

UNSCATHED HERBAL REMEDIES FOR DIABETES: SIMPLE DIETETIC TRICKS CAN DEPART THE NEGATIVES

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ABSTRACT

Diabetes mellitus is a public health problem which leads to serious complications over time and is identified as one of the main threats to human health in the 21st century. Diabetes is one of four priority non-communicable diseases (NCDs) targeted for action by world leaders. Diabetes Mellitus (DM) is a fifth fastest growing disorder and entailing a huge financial burden and multiple medical policy issues. The management of diabetes is still a major challenge. All the existing therapies of diabetes have limited efficacy, confined tolerability and/or significant mechanism based side effects. Thus there is great demand for research on natural products with anti-diabetic properties. Numerous studies have confirmed that the plant drugs and formulations are considered to be less hazardous and free from side effects than the synthetic ones. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purposes around the world. Medicinal plants and phyto-constituents play an important role in the management of diabetes mellitus especially in developing countries where resources are meagre. Additionally, lifestyle and particularly dietary habits play an important role in the development of diabetes. On the other hand, specific individual food groups and diet components such as monounsaturated fatty acids, fruits, vegetables, whole grain cereals, dietary fiber, fish, magnesium and nuts may protect against the development of diabetes, possibly through the amelioration of insulin sensitivity and its anti-inflammatory actions, while consumption of red and processed meats and saturated fat may increase the risk of type 2 diabetes. A comprehensive review was conducted to pile up information about medicinal plants used for the treatment of diabetes along with plant parts used and its active chemical constituents. In this review article, emphasis is also given on the role of diet and life style in the management of diabetes.

KEYWORDS: Diabetes, herbal remedies, dietetic tricks, life style, complications.

INTRODUCTION

Diabetes is a chronic disorder of metabolism of carbohydrates, proteins and fat due to absolute or relative deficiency of insulin secretion and with varying degree of insulin resistance which can be characterized by hyperglycaemia, glycosuria, hyperlipidaemia, and negative nitrogen balance. The World Health Organization (WHO) estimates that globally, high blood glucose is the third highest risk factor for premature mortality, after high blood pressure and tobacco use.^[1] Diabetes was one of the first diseases described, with an Egyptian manuscript from c. 1500 BCE mentioning "too great emptying of the urine". Indian physicians around the same time identified the disease and classified it as *madhumeha* or "honey urine", nothing the urine would attract ants. Type 1 and type 2 diabetes were identified as separate conditions for the first time by the Indian physicians Sushruta and Charaka in 400-500 CE with

type 1 associated with youth and type 2 with being overweight.^[2]

Type 1 diabetes (previously known as insulin-dependent, juvenile or childhood-onset diabetes) is characterized by deficient insulin production in the body. People with type 1 diabetes require daily administration of insulin to regulate the amount of glucose in their blood. If they do not have access to insulin, they cannot survive. The cause of type 1 diabetes is not known and it is currently not preventable. Symptoms include excessive urination and thirst, constant hunger, weight loss, vision changes and fatigue.

Type 2 diabetes (formerly called non-insulin-dependent or adult onset diabetes) results from the body's ineffective use of insulin. Type 2 diabetes accounts for the vast majority of people with diabetes around the world. Symptoms may be similar to those of type 1

diabetes, but are often less marked or absent. As a result, the disease may go undiagnosed for several years, until complications have already arisen. For many years type 2 diabetes was seen only in adults but it has begun to occur in children.

Gestational diabetes (GDM) is a temporary condition that occurs in pregnancy and carries long term risk of type 2 diabetes. The condition is present when blood glucose values are above normal but still below those diagnostic of diabetes. Women with gestational diabetes are at increased risk of some complications during pregnancy and delivery, as are their infants. Gestational diabetes is diagnosed through prenatal screening, rather than reported symptoms.^[3]

Plants are still important sources of medicines, especially in developing countries that still use plant based traditional medicine for their healthcare.^[4] Herbal medicine, also called botanical medicine or phyto medicine, refers to the use of any plant's seeds, berries, roots, leaves, bark, or flowers for medicinal purposes. Long practiced outside of conventional medicine, herbalism is becoming more main stream as up-to-date analysis and research show their value in the treatment and prevention of disease.^[5] Interests in ethno-botanical explorations have been increased in recently at the national and international level. A perusal of the literature reveals that there is still a huge gap in knowledge of ethno-medicine and its scientific validation in this part of the world. Traditional use of plants and plant-parts has been a deep rooted practical knowledge in the culture and livelihood of the people living in the remote parts of the world and has been using different medicinal plants in their daily healthcare practices.

According to the World Health Organization (WHO) about 65-80% of the world's population in developing countries depends essentially on plants and plant derived compounds for their primary health care.^[6] Ayurveda and other traditional medicinal system for the treatment of diabetes describe a number of plants used as herbal drugs. They play an important role as alternative medicine due to less side effects and low cost. Ayurvedic plants provide the best option for search of desired safe and effective medications. Since ancient times, plants have been an exemplary source of medicine. Various Ayurvedic plants have been found to possess significant anti-diabetic property after their preclinical and clinical evaluation. Use of these plants may delay the development of diabetic complications and can correct the metabolic abnormalities through variety of mechanisms. Moreover, during the past few years many experimental studies were carried using aqueous and alcoholic extracts of anti-diabetic plants which explore the new ways of treatment of diabetes mellitus.^[7]

METHODOLOGY

This review article has been prepared from secondary study materials such as published journal articles, review papers, conference papers & reports, technical & theoretical notes, books, & relevant information found from various online sources.

Ethno-botanical Study

Hyperglycemia can be reversed by a variety of measures. Administration of exogenous insulin is the treatment for all type 1 diabetic patients and for some type 2 patients who do not achieve adequate blood glucose control with oral hypoglycemic drugs. Insulin therapy has several drawbacks like insulin resistance, anorexia, brain atrophy and fatty liver in chronic treatment.^[2] Herbal and natural products of folk medicine have been used for centuries in every culture throughout the world. Scientists and medical professionals have shown increased interest in this field as they recognize the true health benefits of these remedies. "Let food be your medicine and let medicine be your food" was advised by the father of medicine, Hippocrates, over two million ago.^[8] There is a new trend in the world to turn back to natural substances to avoid the side effects associated with the synthetic drugs. Many plant species have been used to treat life-threatening diseases like diabetes. A World Health Organization (WHO) study shows that 80% of the world population solely relies on the medicinal plants for their primary health care needs.^[9] In this review article, an attempt has been made to compile the reported hypoglycemic plants available in different scientific journals and may be useful to the health professionals, scientists and scholars working in the field of pharmacology and therapeutics to develop evidence based alternative medicine to cure different kinds of diabetes in man and animals. This review shows the importance and the interest placed on medicinal plants in the drive to demonstrate their anti-diabetic effects and the responsible bioactive agents. This review also covers the common name of a plant, the parts that are commonly used as a remedy sources and extracts.

Analysis of remedies obtained from different plant parts for Diabetes Mellitus.

Family	Scientific name	Common name/ English name	Parts used	Extract types	Active compound	chemical	References
Febaceae	<i>Abrus precatorius</i>	Ratti, Kundumani	Seed, Root, Leaf	Aqueous	-	-	[10,11]
Febaceae	<i>Acacia Arabica</i>	Indian gum arsbic	Seed, Bark	-	Polyphenol, Tannin	-	[10,12,13,14,15,16,17]
Rutaceae	<i>Aegle marmelose</i>	Bael, Golden apple	Seed, Fruit, Leaf	Ethanol, Aqueous	Aegelin 2, Coumarin, Flavonoid, Alkaloid	-	[5,12,18,19]
Liliaceae	<i>Allium cepa</i>	Pyaj, Onion	Bulb	Ethyl ether extracts	S-methyl cysteine sulphoxide, Allyl propyl disulphide	-	[5,10,12,20,21, 22,23]
Liliaceae	<i>Allium sativum</i>	Lahsun, Garlic	Bulb	Ethanol	S-allyl cysteine sulfoxide/allicin,	-	[5,10,12,20,21, 23,24,25]
Aloceae	<i>Aloe vera</i>	Aloe vera	Leaf	Leaf pulp extract	Glucomannan	-	[10,12,19,20,21,25, 26,27,28]
Asphadlanceae	<i>Aloe barbadensis</i>	Barbados aloe	Leaf	-	Lophenol,24-methyl lophenol, 24-ethyle lophenol cycloartenol, 24-methylene cycloartenol	-	[21]
Amaranthaceae	<i>Amaranthus esculentus</i>	-	Whole plant	Oil fraction	-	-	[12,22]
Acanthaceae	<i>Andrographis paniculata</i>	Kalomegh	Leaves	-	Trapenids & steroids	-	[5,18,19,29]
Annonaceae	<i>Annona squamosal</i>	Ata	Leaf and fruit	Ethanol and aqueous	-	-	[12,22]
Moraceae	<i>Artocarpus heterophyllus</i>	Jack fruit	Fruit	Aqueous	Sapogenin	-	[12,30]
Liliaceae	<i>Asparagus racemosus</i>	-	Root	Ethanol, Chloroform, Hexane	-	-	[22]
Meliaceae	<i>Azadirachta indica</i>	Neem	leaf, seed and fruits	Raw leaf extracts	Azadirachtin, Meliacin, Salanin, Nimbin, Valassin Nimbidin,β-sitosterol	-	[5,10,12,18,19,20,21, 24,25,31,32,33,34]
Chenopodiaceae	<i>Beta vulgaris</i>	Beetroot	Entire plant	-	Pectin, Polydextrose	-	[12,14,21]
Brassicaceae	<i>Brassica juncea</i>	Mustard	Seed, Leaf	Aqueous	Isorhamnetin diglcoside	-	[12,13,14]
Brassicaceae	<i>Brassica nigra</i>	-	Seed	Aqueous	-	-	[22,35]
Solanaceae	<i>Capsicum frutescens</i>	Chilli	-	-	Capsaicin	-	[12,13,14,22,36]
Cariaceae	<i>Carica papaya</i>	papaya	fruit	Aqueous extract	Saponin, Tannin, alkaloid, Flavonoid, Anthraquinone, Glycoside	-	[12,13,18,37,38]
Leguminoceae	<i>Cajanus cajan</i>	Pigeon pea	Seed, Leaf	Ethanol	7-phenol-octahydroquinolisin-2-one	-	[12,14,19,21,39]
Apocynaceae	<i>Catharanthus roseus</i>	Red periwinkle / Nayantara	Whole plant	-	Vinculin, Alkaloid	-	[12,31]
Apiaceae	<i>Centella asiatica</i>	Thankuni	Leaf/whole plant	Ethanol leaf extract	Alkaloids, Phenols, Flavonoids, Quinones, Triterpenoids	-	[12,19,40,41]
Lauraceae	<i>Cinnamonum zeylanicum</i>	Cinnamon	Leaf, Bark	-	Cinnamaldehyde	-	[12,13,14]
Apiaceae	<i>Coriandrum sativum</i>	Coriander	Leaf, Seed, Fruit	Aqueous	Alanine	-	[12,42,43,44]
Cucurbitaceae	<i>Coccinia indica</i>	Ivy-gourd	Fruit, Leaf	Alcoholic	B-amyrin, Lupeol, Cucurbitacin B	-	[12,19,45,46]
Zingiberaceae	<i>Curcuma longa</i>	Haldi, Turmeric	Raw turmeric/	Aqueous extract	Curcuminoid	-	[5,7,12,18,21,31,37]

			root			
Apiaceae	<i>Cuminum cyminum</i>	Cumin seed	Seed	-	Aldehyde	[12,14,21]
Ebenaceae	<i>Diospyros lotus</i>	Date plum	Fruit	Aqueous	Phenolic	[12,13]
Moraceae	<i>Ficus racemosa</i>	Jogadumur	Ripe fruits/ Bark		α -amyrin acetate	[18,31,37]
Moraceae	<i>Ficus bengalensis</i>	Banyan tree	Bark	-	Leucopelargonidin	[12]
Moraceae	<i>Ficus carica</i>	Anjir	Leaf, Fruit	-	Invert sugar	[12]
Asclepiadaceae	<i>Gymnema sylvestre</i>	Gurmur, Destroyer of sugar	Leaf	Aqueous, Methanolic	Gymnemic acid, Gymnema saponin	[20,37,47,48,49]
Febaceae	<i>Glycine max</i>	Soya bean	Seed	-	3-O-methyl-D-chiro- inositol	[12,13,14]
Malvaceae	<i>Hibiscus rosa sinensis</i>	-	Flower	Ethanollic		[12,19,50,51,52,56]
Poaceae	<i>Hordeum vulgare</i>	Barley	Seed	-	Beta-glucan	[12]
Crassulaceae	<i>Kalanchoe pinnata</i>	Patharkuchi	Leaf	-	-	[31]
Nymphaeaceae	<i>Nelumbo nucifera</i>	Sacred lotus	Flower	-	Tolbutamide	[12,14,79]
Anacardiaceae	<i>Mangifera indica</i>	Mango tree	Stem, Bark, Fruit, Leaf	Aqueous, Alcoholic	Mangiferin, Phenolics, Flavonoid	[12,18,37]
Lamiaceae	<i>Mentha piperita</i>	Peppermint	Leaf	-	Essential oil, Terpen, Flavonoid. Vanadium, Zinc, Chromium, Copper, Iron, Potassium, Sodium, Nickel	[12,14]
Cucurbitaceae	<i>Momordica charantia</i>	Karela/ Bitter melon	Fruit	Methanolic, Aqueous, Chlorophormic	Charantin, β - sitosterol, cucurbitacin	[10,12,18,28,37,38, 56,65]
Rutaceae	<i>Murraya koenigii</i>	Curry leaf tree	Leaf, Fruit	Fruit juice	Carbazole, alkaloid	[12,13,14]
Musaceae	<i>Musa paradisiaca</i>	Banana	Mature, green fruit	Methanolic extract	Dietary fibre, pectin	[12,18]
Musaceae	<i>Musa sapientum</i>	Sweet banana	Flower	-	Flavonoids, Steroid, Glycosides	[12,13,14,21]
Lamiaceae	<i>Ocimum sanctum</i>	Tulsi/ Holy basil	Leaf	Aqueous, Ethanollic	Eugenol (1-hydroxy-2- methoxy-4- allylbenzene)	[5,10,12,19,21,37,53, 54,55,56,57]
Lauraceae	<i>Persea americana</i>	Avocado	Fruit	Aqueous	Fat, Protein, Vitamin, Mineral	[12,13,14]
Phyllanthaceae	<i>Phyllanthus emblica</i>	Amla/ Amloki	Fruit	Ethanollic extract	Tannoid	[12,18,31]
Piperaceae	<i>Piper betle</i>	Pan	Leaf	Aqueous	-	[12,22,58,59]
Myrtaceae	<i>Psidium guajava</i>	Guava	Leaf, Fruit	Aqueous, Ethanollic	Terpen, Flavonoid, Strictinin, Polysaccharide, Isostrictinin, Pedunculagin	[12,13,18,22,37,51, 60,61,62]
Amaranthaceae	<i>Spinacea oleracea</i>	Palongshak	Whole plant	-	-	[31,63,64,65]
Meliaceae	<i>Swietenia macrophylla king</i>	Mehogony	Seed	Aqueous, Ethanollic	Triterpenoids, Fatty acid, Methyl esters, Aldehydes, Fucosterol, Phytosterols and β -sitosterol	[66,67,68,69,70,71, 72,73,74]
Myrtaceae	<i>Syzigium cumini</i>	Jamun/ Blackberry	Fruit, leaf, seed, bark	Ethanollic extract	Jambosine, Jamboline or Antimellin	[5,18,20,24,37,55]
Febaceae	<i>Tamarindus indica</i>	Tatul tree	Seed, Fruit	Methanolic extract	Flavonoid, Steroid	[12]

Combretaceae	<i>Terminalia catappa</i>	Indian almond	Fruit	Petroleum ether, Methanolic, Aqueous	Phenolics	[12]
Papilionaceae	<i>Trigonella foenum graecum</i>	Methi	seed	Alcoholic, Ethanolic	-	[5,76]
Poaceae	<i>Triticum vulgare</i>	Wheat	Whole plant	-	Albumin	[12,14]
Febaceae	<i>Xanthocercis zambesiaca</i>	Nyala tree	Leaf	-	Fagomine, 4-O-beta-D-glucopyranosylfagomine, Castanosperamine	[12,13,14]
Zingiberaceae	<i>Zingiber officinale</i>	Ginger	Bulb	-	Gingerol, Ethanol	[12,37,77]

PRESENT SITUATION

Diabetes is one of the most challenging public health problems of the 21st century. Each year more and more people live with this condition, which can result in life-changing complications. According to IDF (2015), the Global prevalence of diabetes was 8.8% (7.2-11.4%) in 2015 and it will become 10.4% (8.5-13.5%) in 2040. One in eleven adults in 2015 was affected with diabetes and it will be one in ten adults in 2040. One in two adults with diabetes is undiagnosed. The IDF estimated that, one in seven births is affected by gestational diabetes, 542,000 children have type 1 diabetes and 12% of global health expenditure is spent on diabetes. The 10 top countries in numbers of people suffering from diabetes are India, USA, China, Japan, Indonesia, Egypt, Brazil, Russia, Mexico and Bangladesh.^[1]

One critical feature about the 7th edition of the IDF Diabetes Atlas is that the data shows a continued increase in the prevalence of diabetes. Today, we know that 415 million people (one out of eleven adults) have diabetes and every six seconds a person dies with diabetes. Moreover, every two seconds a new case of diabetes is diagnosed somewhere in the world. This is most alarming and the whole world needs to know about it and take action. If the current trends in diabetes prevalence continue, by 2040 some 642 million people will have diabetes. Given that 75% of all people with diabetes live in low- and middle-income countries.^[3]

FUTURE PROSPECTS

Traditional herbal medicine has been used since ancient time in many parts of the world. The many side effects of insulin therapy and other oral hypoglycemic agents necessitate the use of more effective and safer anti-diabetic drugs. For example, long-term use of Metformin causes diarrhoea, nausea, gas, weakness, indigestion, abdominal discomfort and headache.^[78] Diabetes is still not completely curable by the present anti-diabetic medicines. All the existing therapies however have limited efficacy, confined tolerability and/or significant mechanism based side effects.^[2] Plant based drug are considered to be less toxic and free from side effects than synthetic one. Hence, they play an important role as alternative medicine. Diabetes has been treated with plant medicine since antiquity. Recent scientific

investigation has confirmed the efficacy of many anti-diabetic plant preparations some of which are very effective and relatively non-toxic.^[9] Although many plant species have been validated for their anti-diabetic properties and related complications, there is a need for modern research in the identification of phytochemical compound(s), their target(s) and their modes of action and combination therapy of plant products with synthetic drugs.^[20]

Treatment employing two or more herbs in combination is known as ‘polyherbal therapy’. Polyherbal therapy is said to be a better choice in the treatment of diabetes mellitus having the advantage of producing maximum therapeutic efficacy with minimal side effects. This may provide synergistic and potentiative pharmacological properties within themselves because of presence of vast range of phyto-bioactive constituents. Polyherbal therapy also gives an opportunity to reduce the dose of herbs used for glycemic control in order to avoid the burden of herbal over dose.^[2] To make the therapy cost effective, extensive clinical studies for long-term side effects are a must. A large-scale production of quality plant material and innovative procedures to easily consume these medicinal plant species have to be further validated.^[20]

COMPLICATIONS IN DIABETES MELLITUS

Diabetes is a group of chronic diseases characterized by hyperglycaemia. Chronic hyperglycaemia injures the human body in many different ways. Modern medical care therefore uses a vast array of lifestyle and pharmaceutical interventions aimed at preventing and controlling hyperglycaemia.

One of the chief injuries arising from hyperglycaemia is injury to vasculature, which is classified as either small vascular injury (microvascular disease) or injury to the large blood vessels of the body (macrovascular disease). As medical science advances increasingly toward prevention of complications of diabetes, it is important for clinicians to be familiar with the relationship between diabetes control and vascular injury.^[79] Diabetes involves chronic levels of abnormally high glucose (hyperglycaemia). Many patients, especially those with type 2 diabetes; also have elevated blood pressure (hypertension), chronic high levels of insulin

(hyperinsulinemia) and unhealthy levels of cholesterol and other blood fats (hyperlipidaemia). All of these factors contribute to the long-term complications of diabetes.^[80] Such as:

Complication types	Diseases
Microvascular complications	Eye diseases (diabetic retinopathy, glaucoma, cataracts), diabetic nephropathy, diabetic neuropathy
Macrovascular complications	Cardiovascular disease, cerebrovascular disease, peripheral arterial disease
Micro and macrovascular complications	Diabetic foot ulcer
Acute metabolic complications	Diabetic ketoacidosis, hypoglycaemia, Hyperosmolar hyperglycaemic non-ketotic state
Miscellaneous complications	Impaired thinking, cancer, musculoskeletal disorders, pregnancy complications, insulin shock, emotional difficulties

1. Microvascular Complications of Diabetes

Eye diseases

These include diabetic retinopathy, glaucoma and cataracts. Diabetes is a leading cause of visual impairment and blindness.^[80] Diabetic retinopathy may be the most common microvascular complication of diabetes. It is responsible for ~ 10,000 new cases of blindness every year in the United States alone.^[81] The risk of developing diabetic retinopathy or other microvascular complications of diabetes depends on both the duration and the severity of hyperglycaemia. Development of diabetic retinopathy in patients with type 2 diabetes was found to be related to both the severity of hyperglycaemia and the presence of hypertension in the U.K.^[79] Diabetic retinopathy is the most frequent cause of new cases of blindness among adults aged 20-74 years. Diabetic retinopathy can progress from mild non proliferative abnormalities, to moderate and severe non proliferative diabetic retinopathy, and finally, to proliferative diabetic retinopathy.^[81]

Diabetic nephropathy

Diabetic nephropathy is the leading cause of renal failure in the United States. It is defined by proteinuria of > 500 mg in 24 hours in the setting of diabetes, but this is preceded by lower degrees of proteinuria, called "micro albuminuria." Micro albuminuria is defined as albumin excretion of 30–299 mg/24 hours. Without intervention, diabetic patients with micro albuminuria typically progress to proteinuria and overt diabetic nephropathy. This progression occurs in both type 1 and type 2 diabetes. As many as 7% of patients with type 2 diabetes may already have micro albuminuria at the time they are diagnosed with diabetes. In the European Diabetes Prospective Complications Study, the cumulative

incidence of micro albuminuria in patients with type 1 diabetes was ~ 12% during a period of 7 years. In the UKPDS, the incidence of micro albuminuria was 2% per year in patients with type 2 diabetes, and the 10-year prevalence after diagnosis was 25%.^[79]

Diabetic neuropathy

Diabetic neuropathy is recognized by the American Diabetes Association (ADA) as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes."^[15] As with other microvascular complications, the risk of developing diabetic neuropathy is proportional to both the magnitude and duration of hyperglycaemia, and some individuals may possess genetic attributes that affect their predisposition to developing such complications.^[79] Diabetic peripheral neuropathy (DPN) is one of the most prevalent and complicated conditions to manage among diabetic patients. About 60% to 70% of people with diabetes have mild to severe forms of nervous system damage; resulting in impaired sensation or pain in the feet or hands, slowed digestion of food in the stomach, carpal tunnel syndrome, precursor for foot ulcers, and other nerve problems. Diabetes is the major contributing reason for non-traumatic lower extremity amputations (more than 60% of cases). The most common form of DPN involves the somatic nervous system; the autonomic nervous system may be affected in some patients.

2. Macrovascular complications of diabetes

Diabetes exerts a heavy toll on the vascular system. The hallmark of diabetic macrovascular disease is accelerated by atherosclerosis involving the aorta and large and medium-sized arteries. Macrovascular disease causes accelerated atherosclerosis among diabetics, resulting in increased risk of myocardial infarction, stroke, and lower-extremity gangrene. Macrovascular complications associated with diabetes include cardiovascular, cerebrovascular, and peripheral arterial diseases.

Cardiovascular disease (CVD)

People with diabetes are 2 to 4 times more likely to develop cardiovascular disease (CVD) than those without diabetes. Diabetes increases the risk that an individual will develop cardiovascular disease (CVD). Although the precise mechanisms through which diabetes increases the likelihood of atherosclerotic plaque formation are not completely defined, the association between the two is profound. CVD is the primary cause of death in people with either type 1 or type 2 diabetes.^[82] In fact, CVD accounts for the greatest component of health care expenditures in people with diabetes.^[79]

Cerebrovascular disease

Cerebrovascular disease is a term encompassing many disorders that affect the blood vessels of the central nervous system. These disorders result from either inadequate blood flow to the brain (i.e., cerebral

ischemia) or from haemorrhages into the parenchyma or subarachnoid space of the central nervous system (CNS). Diabetes is also a strong independent predictor of risk of stroke as in coronary artery disease. Patients with type 2 diabetes have a much higher risk of stroke, with an increased risk of 150–400%. Risk of stroke-related dementia and recurrence, as well as stroke-related mortality, is elevated in patients with diabetes.^[79]

Peripheral Arterial Disease

Peripheral arterial disease (PAD) is an atherosclerotic occlusive disease. It is the major risk factor for lower extremity amputations. The abnormal metabolic state accompanying diabetes results in changes in the state of arterial structure and function predisposing people to PAD. The risk of development of PAD increases threefold to fourfold in patients with diabetes mellitus.

3. Diabetic foot ulcers

Diabetic foot ulcers and infections are responsible for >30% of the hospitalisations related to diabetes mellitus. 25% of people with diabetes mellitus are estimated to develop a foot ulcer during their lifetime. Diabetic foot ulceration is also an expensive complication of diabetes mellitus, owing to both medical care and on account of time lost from work and loss of income and financial independence^{[83],[84]}.

4. Acute metabolic complications

Diabetic ketoacidosis

A lack of insulin can force the body to burn fats instead of glucose for energy. The result is a toxic byproduct called ketones, along with severe hyperglycaemia.^[80]

Hyperosmolar hyperglycaemic nonketotic state

This involves severe hyperglycaemia and dehydration.^[80]

Hypoglycaemia

Hypoglycaemia is common in insulin-treated diabetic patients and also occurs occasionally in patients treated with the oral hypoglycaemic sulfonylurea agents. Hypoglycaemia may range from very mild lowering of glycaemia (60-70 mg/dl) with minimal or no symptoms, to severe hypoglycaemia with very low ant levels of glucose (<40 mg/dl) and neurologic impairment.^[80]

5. Miscellaneous complication

Impaired thinking

Many studies have linked diabetes to increased risk of memory loss, dementia, Alzheimer's disease and other cognitive deficits. Recently some researchers have suggested that Alzheimer's disease might be "type 3 diabetes," involving insulin resistance in the brain.^[80]

Cancer

Diabetes increases the risk of malignant tumors in the colon, pancreas, liver and several other organs.^[80]

Musculoskeletal disorders

Conditions ranging from gout to osteoporosis to restless legs syndrome to myofascial pain syndrome are more common in diabetic patients than non-diabetics.^[80]

Pregnancy complications

Diabetes increases the risk of preeclampsia, miscarriage, stillbirth and birth defects.^[80]

Emotional difficulties

Many but not all of the studies exploring connections between diabetes and mental illness have found increased rates of depression, anxiety and other psychological disorders in diabetic patients. In addition to chronic hyperglycaemia, diabetic patients can experience acute episodes of hyperglycaemia as well as hypoglycaemia (low glucose). Severe cases can cause seizures, brain damage and a potentially fatal diabetic coma.^[80]

Insulin shock

This advanced stage of hypoglycaemia is typically due to excessive amounts of insulin medication or certain anti diabetic agents.^[80]

ROLE OF DIET AND LIFE STYLE MANAGEMENT IN DIABETES

Lifestyle management is a fundamental aspect of diabetes care and includes diabetes self-management education (DSME), diabetes self-management support (DSMS), nutrition therapy, physical activity, smoking cessation counselling, and psychosocial care. Patients and care providers should focus together on how to optimize lifestyle from the time of the initial comprehensive medical evaluation, throughout all subsequent evaluations and follow-up, and during the assessment of complications and management of comorbid conditions in order to enhance diabetes care.^[85]

1. Diabetes self-management education and support:

In accordance with the national standards for diabetes self-management education and support, all people with diabetes should participate in diabetes self-management education to facilitate the knowledge, skills, and ability necessary for diabetes self-care and in diabetes self-management support to assist with implementing and sustaining skills and behaviours needed for on-going self-management, both at diagnosis and as needed thereafter. Diabetes self-management education and support should be patient centered, respectful, and responsive to individual patient preferences, needs, and values and should help guide clinical decisions. DSME focuses on supporting patient empowerment by providing people with diabetes the tools to make informed self-management decisions.^[85,86] Diabetes care has shifted to an approach that is more patient centered and places the person with diabetes and his or her family at the centre of the care model, working in collaboration with health care professionals. Patient-centered care is respectful of and responsive to individual patient

preferences, needs, and values. It ensures that patient values guide all decision making.^[85]

2. Nutrition therapy: For many individuals with diabetes, the most challenging part of the treatment plan is determining what to eat and following a food plan. There is not a one-size-fits-all eating pattern for individuals with diabetes. Nutrition therapy has an integral role in overall diabetes management, and each person with diabetes should be actively engaged in education, self-management, and treatment planning with his or her health care team, including the collaborative development of an individualized eating plan.^[85]

Component of a Diabetic Diet

(2006 Position Statement of the American Diabetes Association).

	% of Total Daily Calories Intake	Remarks
Carbohydrate	45 –65 % (55%)	-Type and amount of CHO are both important -Greatest impact on blood sugar
Protein	12 –20 % (15%)	-Patients with nephropathy should limit protein to <10%
Fat	25 –35% (30%)	-Monounsaturated & Omega-3 fatty acids are the best types -Limit Saturated fat to < 7% -Minimize trans-fatty acids

3. Carbohydrates: The optimal and normal carbohydrate to lipid ratio in diet is a major challenge considering its role to prevent chronic diseases such as type 2 diabetes. In a study conducted by Richard et al. it was observed that reduced dietary fat intake and increased intake of carbohydrates prevent the incidence of chronic diseases. Some studies demonstrated that increased intake of carbohydrates reduced the incidence of diabetes.^[88] However, several studies reported that increased carbohydrate intake would decrease HDL levels and increase fasting plasma TG concentrations. These data suggested that increased carbohydrate intake increases the secretion of insulin to maintain insulin homeostasis, and a high carbohydrate intake, leading to insulin secretion, is associated with receiving energy that causes higher levels of insulin after a meal. Insulin secretion with high output may be associated with age-related decline in insulin secretion, resulting in a more rapid development of diabetes. It was reported that dietary fibre, particularly soluble fibre, improves the postprandial glycaemic response and insulin concentration through slowing down the digestion and absorption of food and creating a gel-like substance in

the stomach by several metabolic hormones. Several studies have shown that glycaemic control is improved and LDL cholesterol decreases with relatively high carbohydrate, low fat diets including naturally occurring fibre-rich foods compared with relatively low carbohydrate, higher fat diets. Clinical studies on glycaemic index and glycaemic load also showed that the form and content of carbohydrate and fat intake may be effective in short-term glycaemic response. WHO/FAO recommended to get at least 55% of energy intake from carbohydrate in normal people. Hence, there are no specific carbohydrate guidelines to prevent diabetes.^[87]

By choosing appropriate portions of carbohydrate containing foods and selecting ones that have more fibre and a **lower glycaemic index**, will help to improve blood glucose control. Glycaemic index is a scale (0-100) ranking how quickly a carbohydrate containing food will digest into glucose in our blood. **High GI foods** breakdown quickly whereas **low GI foods** break down slowly. With low GI foods one will feel full longer and body’s insulin has more time to perform its job and remove glucose from the blood.^[89]

GI=glycaemic index

Low GI foods (55 Or Less) Choose most often	Medium GI foods (56-69)	High GI foods (70+) Choose less often
Whole grain	bread Couscous	White bread
Pumpernickel bread	Rye bread	Instant mashed potatoes
Oatmeal	Instant Oatmeal	Rice Krispies
All-Bran cereal	Shredded Wheat	Refined, sweetened cereals
Converted rice	Cream of Wheat	Instant rice
Brown & Basmati rice	Whole grain crackers	Bagels
Bulgur, Barley, Quinoa	Pita bread	Waffles/pancakes – made with white flour
Beans, peas, lentils	Apricot, banana	French fries
Apples, peaches, pears	Cantaloupe	Dried dates/figs
Firm cooked pasta	Long grain white rice	Soda crackers
Grapefruit, oranges	Pineapple, raisins	Sweetened fruit juice
Berries, cherries, grapes	Canned fruit in juice	Parsnips, pumpkin
Kiwi, Mango, Plum	Cranberry juice	Rutabaga, turnip
Avocado	New potatoes	Broad beans
Sweet Potato	Beets	Refried beans
Carrots, broccoli	Sweetened condensed milk	Ice cream
Cauliflower, corn		Soft drinks
Leafy vegetables		
Low fat milk, soy milk, yogurt and cottage cheese	*Adapted from “The GI Diet” Rick Gallop	Glucose

4. Fat: Quality and quantity of dietary fat affect glucose tolerance and insulin sensitivity. A high fat diet may cause glucose intolerance through several mechanisms, including lowering insulin binding to its receptors, degradation of glucose transport, reducing TG synthesis, and accumulation of stored triglycerides in skeletal muscles. The fatty acids composition may be related to insulin function through its effect on composition of membrane's phospholipids, which in turn affect membrane fluidity and insulin signalling.^[87]

A high fat diet is a good predictor of developing IGT in healthy people as well as IGT development to type 2 diabetes. High intake of total fat is associated with increased fasting insulin concentration and decreased insulin sensitivity index.^[87]

Intake of saturated fatty acids, monounsaturated and polyunsaturated fatty acids except for the n-3 fatty acids, led to insulin resistance when consuming a high-fat diet. Epidemiological studies suggested that high intake of saturated fat is associated with the risk of IGT and increased fasting glucose and insulin levels. The higher proportion of saturated fatty acids in serum lipids or phospholipids in muscles associated with higher fasting insulin levels would reduce insulin sensitivity and increase the risk of type 2 diabetes. Higher intake of vegetable fat and PUFA reduces the risk of type 2 diabetes as well as decreased fasting plasma glucose concentration and the two-hour glucose concentration.^[87] In general, trans fats should be avoided.^[85]

5. Protein: There is no evidence that adjusting the daily level of protein ingestion (typically 1–1.5 g/kg body weight/day or 15–20% total calories) will improve health in individuals with diabetic kidney disease, and research is inconclusive regarding the ideal amount of dietary protein to optimize either glycaemic control or CVD risk. Therefore, protein intake goals should be individualized based on current eating patterns. Some research has found successful management of type 2 diabetes with meal plans including slightly higher levels of protein (20–30%), which may contribute to increased satiety. For those with diabetic kidney disease (with albuminuria and/or reduced estimated glomerular filtration rate), dietary protein should be maintained at the recommended daily allowance of 0.8 g/kg body weight/day.^[85]

6. Mediterranean Diet and Diabetes: Mediterranean diet was introduced for the first time in 1960s by Ancel Keys through observing food habits of Mediterranean populations. The Mediterranean dietary pattern emphasizes a consumption of fat primarily from foods high in monounsaturated fatty acids and mainly olive oil and encourages daily consumption of fruits, vegetables, low fat dairy products and whole grains, weekly consumption of fish, poultry, tree nuts, legumes, monthly consumption of red meat, as well as a moderate consumption of alcohol, high ingestion of dietary fibre, antioxidants, polyphenols and magnesium.^[87,90] In

addition, it normally contains meals, but the proportions of macronutrients may vary. There is no single Mediterranean diet, although the dietary patterns in the Mediterranean region have many common characteristics. The Mediterranean diet is one of the best-known food patterns for the human health. The Mediterranean diet has beneficial effects for the prevention of type 2 diabetes. These effects include reduced oxidative stress and insulin resistance. Mediterranean diet can act as an anti-inflammatory dietary pattern able to maintain or treat chronic diseases, such as type 2 diabetes.^[87]

7. Obesity management: There is strong and consistent evidence that obesity management can delay the progression from prediabetes to type 2 diabetes and may be beneficial in the treatment of type 2 diabetes. In overweight and obese patients with type 2 diabetes, modest and sustained weight loss has been shown to improve glycaemic control and to reduce the need for glucose-lowering medications. Small studies have demonstrated that in obese patients with type 2 diabetes more extreme dietary energy restriction with very low-calorie diets can reduce A1C to 6.5% (48 mmol/mol) and fasting glucose to 126mg/dL (7.0mmol/L) in the absence of pharmacological therapy or on-going procedures. Body weight management is important for overweight and obese people with type 1 and type 2 diabetes. Lifestyle intervention programs should be intensive and have frequent follow-up to achieve significant reductions in excess body weight and improve clinical indicators. There is strong and consistent evidence that modest persistent weight loss can delay the progression from prediabetes to type 2 diabetes and is beneficial to the management of type 2 diabetes.^[85]

8. Physical activity: Physical activity is a general term that includes all movement that increases energy use and is an important part of the diabetes management plan. Exercise is a more specific form of physical activity that is structured and designed to improve physical fitness. Both physical activity and exercise are important. Exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being. Physical activity is as important for those with type 1 diabetes as it is for the general population, but its specific role in the prevention of diabetes complications and the management of blood glucose is not as clear as it is for those with type 2 diabetes.^[85]

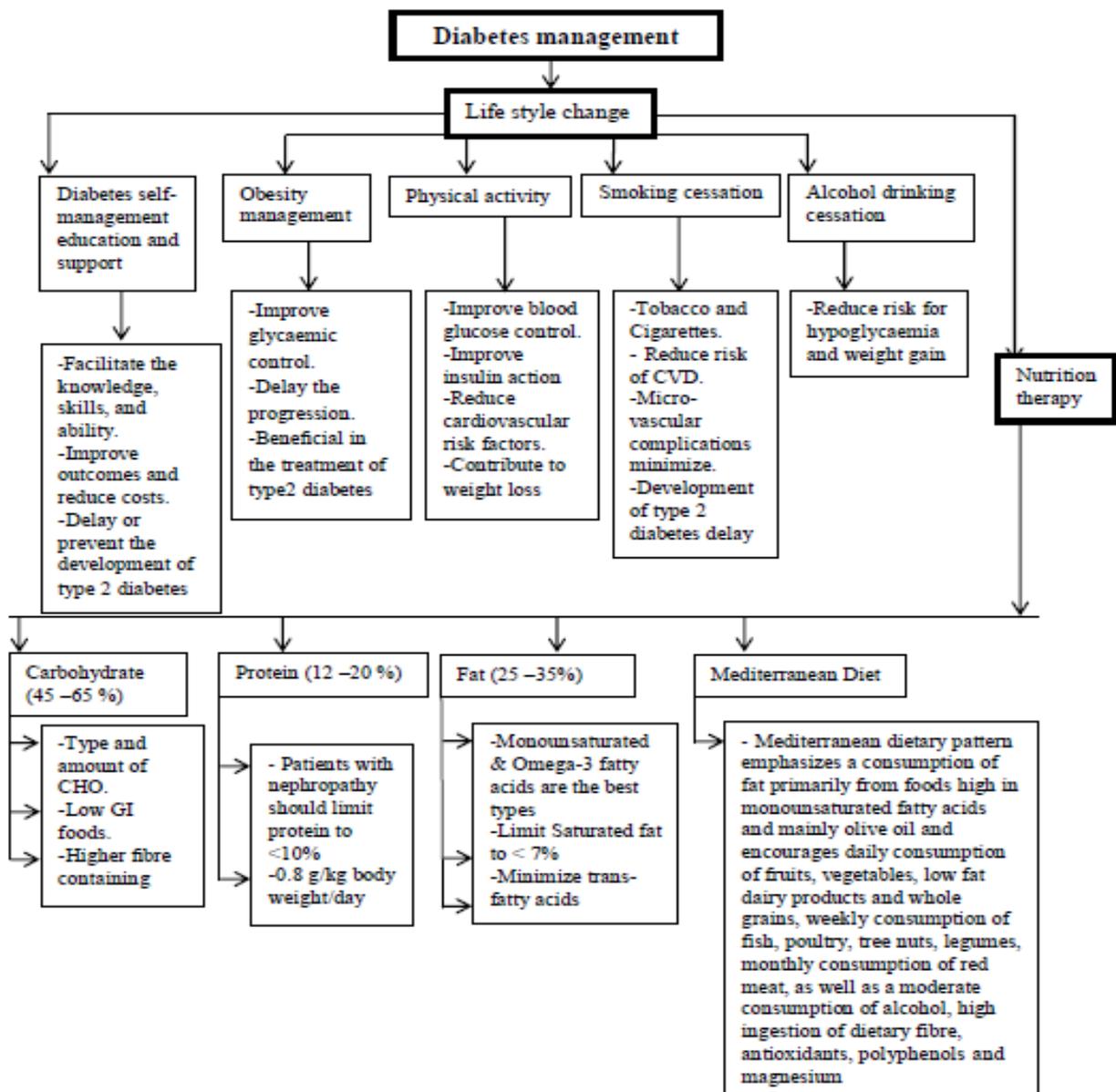
Numerous studies have shown an association between physical inactivity and the incidence of type 2 diabetes. Exercise has a significant role in the regulation of blood glucose, metabolism of proteins and fats, improvement of insulin action, prevention of complications of diabetes, improvement of muscle flexibility and strength, beneficial effects on the cardiovascular system activity is beneficial for the mental state of individual, because it increases the energy of the human body, improves self-

esteem and decreases depression. The basis of a useful exercise is its intensity, duration and frequency. The duration of the exercise should be 30 minutes in the beginning, starting with 5-10 minutes of warm-up and ending always with recovery exercises. The lower frequency recommended is 3 times/wk. Usually low intensity and long-duration exercise programs are considered as the most appropriate and safe patterns for patients with diabetes.^[87]

9. Smoking cessation: Tobacco And Cigarettes: Results from epidemiological, case-control, and cohort studies provide convincing evidence to support the causal link between cigarette smoking and health risks. Recent data show tobacco use is higher among adults with chronic conditions. Other studies of individuals with diabetes consistently demonstrate that smokers (and

people exposed to second hand smoke) have a heightened risk of CVD, premature death, and micro-vascular complications. Smoking may have a role in the development of type 2 diabetes. One study in smokers with newly diagnosed type 2 diabetes found that smoking cessation was associated with amelioration of metabolic parameters and reduced blood pressure and albuminuria at 1 year.^[85]

10. Psychosocial issues- Emotional well-being is an important part of diabetes care and self-management. Psychological and social problems can impair the individual's or family's ability to carry out diabetes care tasks and therefore potentially compromise health status.^[85]



Diet chart for dietetic patient (Thin person)

Time	Diet content
7.00-8.00 am	Wheat flour bread- 90 gm (3 small sized) Egg- 1 or lentils- 15 gm vegetable- Spinage, cauliflower, capsicums, cucumber, papaya, tomato, radish, chilli, gourd (any one from this)
11.00 am	Parched rice (1 cup), biscuit etc- 30 gm Fruits- coconut water, emblica, hog plum, lemon, rose apple, grape fruit, star fruit, melon etc (any one from this)
1.00-2.00 pm	plain rice 300 gm (2.5 cup) Meat or fish- 60 gm (2 pieces) Lentils- 20 gm (1 medium sized cup) Vegetables-spinach, capsicum, cauliflower, chilli, gourds, cucumber, papaya, turnip, tomato, pumpkin, drumstick (any one from this) or potato, sweet pumpkin, edible root, beetroot, kidney bin, cowpea (any one from this)
5.00-6.00 pm	Parched rice (1 cup), biscuit etc- 30 gm
8.00-9.00 pm	Wheat flour bread-120 gm (4 small sized) or plain rice- 2 cup Meat or fish- 60 gm (2 pieces) Lentils- 20 gm (1 medium sized cup) vegetable- Spinage, cauliflower, capsicums, cucumber, papaya, tomato, radish, chilli, gourd (any one from this)

Note- Calory-1800 (Carbohydrate-280 gm ;Protein- 70 gm ; Fat- 46 gm)

Diet chart for dietetic patient (Obese person)

Time	Diet content
Breakfast	Wheat flour bread- 2 small sized Egg- 1 (without egg yolk) or lentils
Lunch	Parched rice (1 cup) Meat (2 pieces) or fish (1 piece) or lentil or vegetable
Supper	Wheat flour bread- 3 small sized Lentils or vegetables or fish or meat (1 pece)
Fruits	Banana (1) or mango (1 piece) or jackfruit (3/4 pieces) or small apple (1) or orange (1)
Milk	1 glass (without milk cream)

CONCLUSIONS

The present study reveals that traditional ethno-botany practices still play a very important role. Ethno-botany practices not only play an important role of primary health care but also play a vital role of conservation of phytodiversity and cultural diversity. Based on the observations, it is expected that the results of this study will lead to phytochemical and pharmacological investigations. The result could also serve as a base to develop phytomedicine in combating diseases. However, many other active agents obtained from plants have not been well characterized. More investigations must be carried out to evaluate the mechanism of action of medicinal plants with anti-diabetic effect.

REFERENCES

1. IDF Diabetes Atlas, Seventh Edition, 2015.
2. Amin *et al.*, Histomorphology of the pancreas and liver treated with herbal extracts in alloxan induced diabetic mice; MS thesis; department of Anatomy and Histology; FVS, BAU, Mymensingh-2202.
3. World Health Organization 2016; Global Report on Diabetes.
4. Salim, A. A., Chin, Y.W. and Kinghorn, A.D. Drug discovery from plants. In: K.G. Ramawat and J.M. Merillon (Eds.), *Bioactive Molecules and Medicinal Plants*, pp. 1-24. Cambridge, England: Cambridge University Press, 2008.
5. Amarnath shukla *et al.*, Anti-diabetic Herbal Drugs: A Review, *International Ayurvedic Medical Journal*, January – 2015; 3(1): 134-147. www.iamj.in.
6. Sharma KA, Kumar R, Misra A, Gupta R. Problem associated with clinical trials of Ayurvedic medicines. *Rev Bras Farmacogn Braz J Pharmacogn*, 2010; 20: 276-281.
7. Yuwraj *et al.*, Anti-Diabetic Activity of Aqueous and Alcoholic Extracts of Ayurvedic Medicinal Plants; *Critical Review on Animal Studies*, *International Journal of Innovative Pharmaceutical*

- Sciences and Research, 2015; 3(12): 1705-1718. www.ijpsr.com.
8. Otari K V et al., Spinacia Oleracea Linn: A Pharmacognostic And Pharmacological Overview, International Journal of Research in Ayurveda & Pharmacy, Sep-Oct 2010; 1(1): 78-84.
 9. Piero et al., Herbal Management of Diabetes Mellitus: A Rapidly Expanding Research Avenue, International Journal of Current Pharmaceutical Research, 2012; 4(2): 1-4.
 10. Chandraprakash Dwivedi et al., Anti-diabetic Herbal Drugs and Polyherbal Formulation Used For Diabetes: A Review, the Journal of Phytopharmacology, 2013; 2(3): 44-51.
 11. Razia Parveen et al., A review on Anti-diabetic Angiospermic plants from the regions of Uttarakhand, India, IOSR Journal of Pharmacy, Oct. 2016; 6(10): 14-61. www.iosrphr.org.
 12. ANM Mamun-or-Rashid et al., A review on medicinal plants with anti-diabetic activity, Journal of Pharmacognosy and Phytochemistry, 2014; 3(4): 149-159. www.phytojournal.com.
 13. Vikrant A, Sharma R. A Review on Fruits Having Anti-Diabetic Potential. Journal of Chemical and Pharmaceutical Research. J Chem Pharm Res, 2011; 3(2): 204-212.
 14. Makheswari MU, Sudarsanam D. Database on Anti-diabetic indigenous plants of Tamil Nadhu, India. Int J Pharma Sci Res, 2012; 3(2): 287-293.
 15. V. V. Rajesham, Ravindernath. A, D. V.R.N. Bikshapathi. A review on medicinal plant and herbal drug formulation used diabetes mellitus, Indo American Journal of Pharmaceutical Research, 2012; 2(10).
 16. Philips AO, Philips GO. Biofunctional behaviour and health benefits of a specific Gum Arabic. Food hydrocoll, 2011; 25(2): 165-169.
 17. Fattaneh Hashem Dabaghian et al., Presenting anti-diabetic plants in Iranian traditional medicine, Journal of Diabetes and Endocrinology, November 2012; 3(5): 70-76. <http://www.academicjournals.org/JDE>.
 18. Aswini Kumar et al., Review of Flora Of Anti-Diabetic Plants Of Puducherry Ut”, International Journal of Applied Biology and Pharmaceutical Technology, Oct - Dec -2011; 2(4): 455-462. www.ijabpt.com.
 19. Radhika S et al., A review on ethnic flora with antihyperglycemic efficacy, International Journal of Herbal Medicine, 2013; 1(4): 55-62. www.florajournal.com.
 20. Ayesha Noor et al., Current update on anti-diabetic biomolecules from key traditional Indian medicinal plants, Current Science, 25 March 2013; 104(6): 721-727.
 21. M.Uma Makheswari et al., Database on Antidiabetic indigenous plants of Tamil Nadhu, India, International Journal of Pharma Sciences and Research (IJPSR), February 2012; 3(2): 287-293.
 22. Abu Zaffar Shibly et al., A comprehensive review on ethno pharmacological antidiabetic potential of traditional ayurvedic plants of Bangladesh, Journal of Pharmacognosy and Phytochemistry, 2015; 4(1): 107-112. www.phytojournal.com.
 23. Ripunjoy Bordoloi et al., A Review on Herbs Used in the Treatment of Diabetes mellitus, Journal of Pharmaceutical, Chemical and Biological Sciences, Jun-August 2014; 2(2): 86-92. <http://www.jpCBS.info>.
 24. Azar Hosseini et al., Pancreatic beta cell protection/regeneration with phytotherapy, Brazilian Journal of Pharmaceutical Sciences, jan./mar., 2015(1): 1-16.
 25. Makwana A R et al., A Review on Medicinal Plants of Gujarat with Anti-diabetic Potential, International Journal of Pharmacognosy and Phytochemical Research, 2016; 8(1): 167-173. www.ijppr.com.
 26. R. POTHURAJU et al., Hypoglycemic and hypolipidemic effects of Aloe vera extracts preparation: A review, PHYTOTHERAPY RESEARCH, Phytother. Res. Published online in Wiley Online Library (wileyonlinelibrary.com) DOI: 10.1002/ptr.5532. 2015.
 27. SAGHIR A. JAFRI et al., Hypoglycemic Effect of Aloe Vera in Allaxon induced albino rats, Medical Journal of Islamic World Academy of Sciences, 2011; 19(3): 127-130.
 28. Mentreddy SR., Mohamed AI., Rimando AM. Medicinal plants with hypoglycemic/anti-hyperglycemic properties: a review, IMIDA, AAIC, 2005; 341-353.
 29. Ramya Premanath et al., Antidiabetic and Antioxidant potential of Andrographis paniculata Nees. Leaf ethanol extract in streptozotocin induced diabetic rats, Journal of Applied Pharmaceutical Science, January, 2015; 5(01): 69-76. <http://www.japsonline.com>.
 30. Ayodhya S et al., Hypoglycaemic activity of different extracts of various herbal plants Singh. Int J Ayurveda Res Pharm, 2010; 1(1): 212-224.
 31. A.H.M. Mahbubur Rahman, Ethno-Botanical Survey of Anti-Diabetic Medicinal Plants Used by the Santal Tribe of Joypurhat District, Bangladesh, International Journal of Research in Pharmacy and Biosciences, June 2015; 2(5): 19-26.
 32. Prabhakar Patil et al., Antidiabetic Activity of Alcoholic Extract of Neem (Azadirachta Indica) Root Bark, National Journal of Physiology, Pharmacy & Pharmacology, 2013; 3(2): 142-146.
 33. Thanasekaran Jayakumar et.al., Experimental and Clinical Pharmacology of Andrographis paniculata and Its Major Bioactive Phytoconstituent Andrographolide, Evidence-Based Complementary and Alternative Medicine, 2013; Article ID 846740: 16.
 34. Muthulinggam Nishan et al., Pharmacological and non-pharmacological activity of Azadirachta indica (Neem)-A review, International Journal of Biosciences, 2014; 5(6): 104-112.

35. Anand P, Murali KY, Tandon V, Chandra R, Murthy PS. Preliminary studies on antihyperglycemic effect of aqueous extract of *Brassica nigra* (L.) Koch in streptozotocin induced diabetic rats. *Indian J Exp Bioi*, 2007; 45: 696-701.
36. Islam MS, Choi H. Dietary red chilli (*Capsicum frutescens* L.) is insulinotropic rather than hypoglycemic in type 2 diabetes model of rats. *Phytother Res*, 2008; 22(8): 1025-1029.
37. Banshidhar Behera et al., Current Researches on Plants Having Antidiabetic Potential: An Overview, Research and Reviews: *Journal of Botanical Sciences, RRJBS*, April – June, 2013; 2(2): 4-17.
38. Izharul H. and Khatoon S., Effect of *Momordica charantia* (bitter melon) tablets in diabetes mellitus: Type 1 and Type 2, *Prime Research on Medicine*, 2012; 2(2): 72-74.
39. Ijomone Oghogho Rosalie and Ekpe EL, Antidiabetic potentials of common herbal plants and plant products: A glance, *International Journal of Herbal Medicine*, 2016; 4(4): 90-97. www.florajournal.com.
40. Nneka N. Uchegbu et al., Germinated Pigeon Pea (*Cajanus cajan*): a novel diet for lowering oxidative stress and hyperglycemia, *Food Science & Nutrition*, 2016; 4(5): 772–777.
41. Ghosh K. et al., Hypoglycemic And Hypolipidemic Potential of *Centella asiatica* Ethanolic Extract on Cadmium Intoxicated Albino Rats, *International Journal of Recent Scientific Research*, July 2015; 6(7): 5327-5332. <http://www.recentscientific.com>.
42. Rahman et al., Antidiabetic Activity of *Centella asiatica* (L.) Urbana in Alloxan Induced Type 1 Diabetic Model Rats, *Journal of Bio-Science*, January 2011; 19: 23-27. <http://www.banglajol.info/index.php/JBS/index>.
43. Abderrahmane A, Soumia ZA, Zafar H. Israili B, Badiia L: Hypoglycemic and hypolipidemic effects of *Coriandrum sativum* L. in Meriones shawi rats. *J Ethnopharmacol*, 2011; 137: 652–61.
44. Momin et al., *Coriandrum Sativum*-Review Of Advances In Phytopharmacology, *International Journal of Pharmaceuticals Sciences and Research, IJPSR*, 2012; 3(5): 1233-1239. www.ijpsr.com.
45. Naquvi et al., Antidiabetic Activity Of Aqueous Extract Of *Coriandrum Sativum* L. Fruits In Streptozotocin Induced Rats, *International Journal of Pharmacy and Pharmaceutical Sciences*, 4(1): 239-240.
46. Ravikant et al., Effect of *Coccinia Indica* Leaf Extract on Diabetic Neuropathy Pain in Rats, *European Journal of Pharmaceutical and Medical Research*, 2016; 3(1): 415-420. www.ejpmr.com.
47. Sahane et al., Phytochemical And Pharmacological Investigation Of *Coccinia Indica* Fruit Extract For Anti-Diabetic Activity, *World Journal of Pharmacy and Pharmaceutical Sciences*, 2014; 3(11): 587-600. www.wjpps.com.
48. Ahmed, A. B. A., Rao, A. S. and Rao, M. V., In vitro callus and in vivo leaf extract of *Gymnema sylvestre* stimulate β -cells regeneration and anti-diabetic activity in Wistar rats. *Phytomedicine*, 2010; 17: 1033–1039.
49. Aralelimath, V.R.; Bhise, S.B. Anti-diabetic effects of *Gymnema sylvestre* extract on streptozotocin induced diabetic rats and possible β -cell protective and regenerative evaluations. *Dig. J. Nanomater. Biostruct.*, 2012; 7: 135-142.
50. Mishra P.K. et al., Antidiabetic and Hypolipidemic Activity of *Gymnema sylvestre* in Alloxan Induced Diabetic Rats, *Global J. Biotech. & Biochem*, 2009; 4(1): 37– 42.
51. Ekta Singh Chauhan et al., Evaluation of Hyperglycemic and Hyperlipidemic Mitigating Impact of *Hibiscus rosa sinensis* (Gudhal) Flower in Type II Diabetes Mellitus Subjects, *International Journal of Applied Biology and Pharmaceutical Technology*, April-June-2016; 7(2): 223-228. www.ijabpt.com.
52. Arumugam G, Manjula P. and Paari N. A review: Anti diabetic medicinal plants used for diabetes mellitus. *Journal of Acute Disease*, 2013; 196-200. www.jadweb.org.
53. Subbarao M. and Basha D. P. Antidiabetic, Hypolipidemic and Histopathological Studies of Ethanolic Leaves Extract of *Hibiscus rosa sinensis* in Alloxan Mono Hydrate Induced Diabetic Rats. *World Journal of Pharmacy and Pharmaceutical Sciences*, 2015; 43: 1064-1074.
54. Khan M.R.I., Antidiabetic Effects of the Different Fractions of Ethanolic extracts of *Ocimum sanctum* in Normal and Alloxan Induced Diabetic Rats, *J. Sci. Res.*, 2010; 2(1): 158-168.
55. Patil R.N., Patil R.Y., Ahirwar B. and Ahirwar D., Isolation and characterization of ant-diabetic component (bioactivity-guided fractionation) from *Ocimum sanctum* L. (Lamiaceae) aerial part. *Asian Pac J Trop Med*, 2011; 4(4): 278-282.
56. Rakhi Mishra et al., A review on herbal antidiabetic drugs, *Journal of Applied Pharmaceutical Science*, 2011; 01(06): 235-237. www.japsonline.com.
57. Rawat Mukesh et al., Medicinal Plants with Antidiabetic Potential - A Review, *American-Eurasian J. Agric. & Environ. Sci.*, 2013; 13(1): 81-94.
58. Khan V, Najmi AK, Akhtar M, Aqil M, Mujeeb M, Pillai KK. A pharmacological appraisal of medicinal plants with antidiabetic potential. *Journal of Pharmacy and Bioallied Sciences*, 2012; 4(1): 27– 42.
59. Arambewela LS, Arawwawala LD, Ratnasooriya WD. Antidiabetic activities of aqueous and ethanolic extracts of *Piper betle* leaves in rats. *J Ethnopharmacol*, 2005; 102: 239-245.
60. Santhakumari P, Prakasam A, Pugalendi KV. Antihyperglycemic activity of *Piper betle* leaf on streptozotocin-induced diabetic rats. *J Med Food*, 2006; 9: 108-112.
61. Chauhan A, Sharma PK, Srivastava P, Kumar N, Duehe R. Plants having potential antidiabetic

- activity: a review. *Der Pharm Lett*, 2010; 2(3): 369-387.
62. Rai PK, Mehta S, Watal G. Hypolipidemic & hepatoprotective effects of *Psidium guajava* raw fruit peel in experimental diabetes. *Indian J Med Res*, 2010; 131: 820-824.
 63. Huang CS, Yin MC, Chiu LC. Antihyperglycemic and antioxidative potential of *Psidium guajava* fruit in streptozotocin-induced diabetic rats. *Food Chem Toxicol*, 2011; 41: 2189-2195.
 64. Gomathi V, Jayakar B, Kothai R, Ramakrishnan G. Antidiabetic activity of leaves of *Spinacia oleracea* Linn. In Alloxan induced diabetic rats. *J Chem Pharm Res*, 2: 266-274, 2010.
 65. Ananta Swargiary et al., Ethno-Botanical Study of Anti-Diabetic Medicinal Plants used by the Local People of Kokrajhar District of Bodoland Territorial Council, India, *Journal of Medicinal Plants Studies*, 2013; 1(5): 51-58. www.plantsjournal.com.
 66. Dutta, et al., Regeneration of pancreatic β -cells on streptozotocin induced diabetic rats under the effect of *Swietenia macrophylla* seeds, *International Journal of Green Pharmacy*, October-December 2012; 6: 336-339.
 67. Mayur R. Bhurat et al., *Swietenia mahagoni* Linn. – A Phytopharmacological Review, *Asian Journal of PHARMACUETICAL RESEARCH*, 2011; 1(1): 1-4. www.ajprjournal.com.
 68. Kalaivanan, K.; Pugalendi, K.V. Antihyperglycemic effect of the alcoholic seed extract of *Swietenia macrophylla* on streptozotocin-diabetic rats. *Pharmacognosy Res*. 2011, 3: 67–71.
 69. Dutta, M.; Biswas, U.K.; Chakraborty, R.; Banerjee, P.; Maji, D.; Mondal, M.C.; Raychaudhuri, U. Antidiabetic and antioxidant effect of *Swietenia macrophylla* seeds in experimental type 2 diabetic rats. *Int. J. Diabetes Dev. Ctries.*, 2013; 33: 60–65.
 70. Habsah Abdul Kadir et al., Biological Activities and Phytochemicals of *Swietenia macrophylla* King, *Molecules*, 2013; 18: 10465-10483. www.mdpi.com/journal/molecules.
 71. Eid et al., A Review On The Phytopharmacological Effect Of *Swietenia Macrophylla*, *International Journal of Pharmacy and Pharmaceutical Sciences*, 2013; 5(3): 47-53.
 72. Mohd AH, Mun FY, Sook YH, Chung PL, Mohd ZA, Amirin S. Antihyperglycaemic activity of *Swietenia macrophylla* king (meliaceae) seed extracts in normoglycaemic rats undergoing glucose tolerance tests. *Chinese Medicine*, 2013; 8: 11.
 73. SMM Mahid-Al-Hasan et al., Effect of Ethanolic Extract of *Swietenia mahagoni* Seeds on Experimentally Induced Diabetes Mellitus in Rats, *Faridpur Medical College Journal*, July 2011; 6(2).
 74. Sukardiman et al., Antidiabetic Activity of Dry Extracts of *Swietenia Mahagoni* Seeds in Alloxan-Induced Diabetic Balb/C, *World Journal of Pharmaceutical Research*, 2017; 6(2): 1334-1339. www.wjpr.net.
 75. Kumar et al., Effect of fenugreek seeds on glycemia and dyslipidemia in patients with type 2 diabetes mellitus, *International Journal of Medical Science and Public Health*, 2015; 4(7): 997-1000.
 76. Iranloye B.O., Arikawe A.P., Rotimi G., Sogbade A.O., Anti-diabetic and anti-oxidant effects of *Zingiber officinale* on alloxan induced and insulin-resistant diabetic male rats, *Niger J Physiol Sci*, 2011; 26(1): 89-96.
 77. Uma Makheswari M and Sudarsanam D, *Phytomedicine for Diabetes mellitus: An overview*, *Research in Pharmacy*, 2011; 1(4): 28-37. www.researchinpharmacy.com.
 78. Narayan et al., Diabetes and Indian Traditional Medicines an Overview, *International Journal of Pharmacy and Pharmaceutical Sciences*, 2012; 4(3): 45-53.
 79. Michael J. Fowler, MD, Diabetes foundation, *Clinical Diabetes*, 2011; 29(3).
 80. Samreen Riaz, *Diabetes mellitus*, *Scientific Research and Essay*, May, 2009; 4(5): 367-373. <http://www.academicjournals.org/SRE>.
 81. Fong DS, Aiello LP, Ferris FL 3rd, Klein R: Diabetic retinopathy. *Diabetes Care*, 2004; 27: 2540–2553.
 82. Paterson AD, Rutledge BN, Cleary PA, Lachin JM, Crow RS: The effect of intensive diabetes treatment on resting heart rate in type 1 diabetes: the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study. *Diabetes Care*, 2007; 30: 2107–2112.
 83. Ranjit Unnikrishnan, Ranjit Mohan Anjana and Viswanathan Mohan, *Diabetes mellitus and its complications in India*, *Nature Reviews, Endocrinology*, June 2016; 12: 357-370. www.nature.com/nrendo.
 84. Cavanagh, P. et al. Cost of treating diabetic foot ulcers in five different countries. *Diabetes Metab. Res. Rev*, 2012; 28(Suppl. 1): 107–111.
 85. American Diabetes Association; *Diabetes Care*, January 2017; 40(Suppl 1).
 86. Marrero DG, Ard J, Delamater AM, et al. Twenty-first century behavioral medicine: a context for empowering clinicians and patients with diabetes: a consensus report. *Diabetes Care*, 2013; 36: 463–470.
 87. Rahati S et al, Food Pattern, Lifestyle and Diabetes Mellitus, *Int J High Risk Behav Addict*, March, 2014; 3(1): e8725.
 88. Salas-Salvado J, Martinez-Gonzalez MA, Bullo M, Ros E. The role of diet in the prevention of type 2 diabetes. *Nutr Metab Cardiovasc Dis*, 2011; 21(Suppl 2): 32–48.
 89. Eating Plan for Type 2 Diabetes, Ottawa Cardiovascular Centre, December 2010. www.cvtoolbox.com.
 90. Kastorini CM, Panagiotakos DB. Mediterranean diet and diabetes prevention: Myth or fact? *World J Diabetes*, 2010; 1(3): 65–76.