Application of Bioactive Molecules in the Treatment and Management of Type-1 Diabetic Disease

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ABSTRACT:

The following is a summary of bioactive chemicals that have been described by researchers based on experimental or clinical antidiabetic data and used in traditional medical systems. Diabetes mellitus is one of the most common non-communicable diseases in the world. A thorough investigation was carried out to gather information on ayurveda, homoeopathic, unani, yoga, and other therapies. It is a metabolic dysfunction disease of the endocrine system that affects over 10% of the world's population, with the number of those affected growing by the day. The scientific and family names, plant parts and test model employed, degree of hypoglycemic activity, and active chemical compounds are all available in the profiles. All bioactive treatments have been demonstrated to be beneficial in the treatment of diabetic complications and in lowering blood glucose levels in diabetics with DBT-1. Natural oral treatment also significantly lowered glucose levels and insulin requirements in diabetic-1 patients, but more clinical research is needed to determine the exact mechanism.

Keywords: Diabetes Mellitus; Medicinal Plant; anti-diabetic bioactive molecules, ayurveda, homoeopathic, unani, yoga autoimmune, Cardiomyopathy, nephropathy, inflammation, neuropathy, and retinopathy

INTRODUCTION

The diabetes epidemic is causing a major financial problem all across the world. Despite the fact that many countries now have improved healthcare facilities, the rate of DBT-1 increase in industrialised, middle, and low-income countries continues to rise. DBT-1 promotes early death and a variety of health problems. It is posing a significant threat to global prosperity. Many sophisticated medications, such as sulphonylureas, biguanides, alpha-glucosidase inhibitors, and thiazolidinediones, are utilised to treat diabetic conditions in current times and

have shown to be beneficial in lowering hyperglycemia. Other current techniques are being utilised to find and grow a new class of pharmaceuticals known as incretin mimetics, Amylin analogues, GIP analogues, Peroxisome proliferator-activated receptors, and dipeptidyl peptidase-4 inhibitors as possible diabetes treatment targets. Ayurvedic therapy, for example, is a popular and widely utilised strategy for treating DBT-1 sickness. Ayurvedic medicine is based on the use of herbal plants (http://www.idf.org/diabetesatlas 2014, http://mdrf.in 2014). These herbal plants contain bioactive chemicals

that stimulate and lower blood sugar levels both directly and indirectly. As a result, the discovery and clinical testing of bioactive compounds from plants has changed drug discovery research and led to the development of diabetes treatment. The review article examines the disease's present statistical popularity, as well as the benefits and limitations of commercially accessible medications, with a focus on rising trends. Furthermore, the crucial areas in clinical diabetology are examined, including the future of statins, nanotechnology, and stem cell technology as next-generation treatments, as well as why herbal formulations are such a popular choice for diabetes medication and control. We discussed the causes and treatments of diabetic disease, as well as the fundamental concepts of various therapeutic systems and yoga approaches (Joshi et al., 2003).

Traditional medicine based on plant extracts has proven to be more affordable and effective in clinical trials. They have fewer side effects than contemporary medications. According to the literature, the pharmaceutical industry has paid much more attention to the use of phytochemical elements in medicinal plants. Secondary metabolites from plants, such as steroids, alkaloids, phenolics, lignans, carbohydrates, and glycosides, are small molecules or macromolecules biosynthesized in plants that have a variety of biological properties beneficial to humans, such as anti-allergic, anticancer, antimicrobial, anti-inflammatory, antidiabetic, and antioxidant properties. Diabetes mellitus is a chronic condition caused by metabolic abnormalities in pancreas cells with hyperglycemia.

Diabetes mellitus (DM) is a metabolic condition caused by abnormalities in insulin secretion, insulin action, or both. It is characterized by persistent hyperglycemia and problems in carbohydrate, lipid, and protein metabolism. Long–term damage, malfunction, and failure of many organs are effects of diabetes mellitus. There are three forms of diabetes mellitus (Mohanand et al., 2006).

INSULIN DEPENDENT

Mellitus (Diabetes Mellitus) is a kind (IDDM). It's also called juvenile-onset diabetes or type DBT-1, and it affects 5-10% of people. It's caused by cellular-mediated autoimmune destruction of pancreatic cells. The condition can strike persons of any age group, but it is most common in children and young adults. Insulin injections must be given on a regular basis to keep blood glucose levels under control. The pace of cell breakdown varies, with newborns and youngsters experiencing rapid degradation while adults experience slower cell degeneration. Children and young people can develop ketoacidosis, while others can develop mild fasting hyperglycemia that can progress to severe hyperglycemia or ketoacidosis in reaction to stress or infection (American Diabetes Association 2001). Other autoimmune disorders such as Grave's disease, vitiligo, celiac sprue, autoimmune hepatitis, myasthenia gravis, Hashimoto's thyroiditis, Addison's disease, and pernicious anaemia are more common in these patients (Kahanovitz et al., 2017). People of African and Asian heritage are more likely to develop this kind of diabetes, which has a hereditary pattern (Reddy et al., 2000). Table 1 shows the disease's classification and the numerous consequences that come with it.

Idiopathic Diabetes

A small percentage of DBT-1individuals, usually of Asian and African origin, have no known cause. Ketoacidosis occurs in episodes, and the level of insulin insufficiency fluctuates between episodes. Idiopathic diabetes is caused by a genetic predisposition, and the necessity for insulin replacement therapy is determined by the patient's condition (Reddy et al., 2000).

Noninsulin Dependent

Mellitus (Diabetes Mellitus) is a kind (NIDDM). It's also known as adult-onset diabetes, and it's responsible for 90–95 percent of all diabetes cases. Obesity, insulin resistance, and dyslipidemia are all major metabolic disorders that have resulted in a DBT-2 epidemic (Moller et al., 2001). Oral hypoglycemic medications and dietary changes are used to treat this form of diabetes. Insulin resistance, as well as a reduction in insulin secretion, plays a role in the development of disease. DBT-2 diabetes is the most common type of diabetes and the fourth largest cause of death in developed nations, with a twofold increased risk of death and a two- to fourfold greater risk of coronary heart disease and stroke (McKinlay et al., 2000).

Gestational Diabetes Mellitus (GDM)

It's described as any degree of glucose intolerance that leads to hyperglycemia of varying severity and is discovered during pregnancy. GDM, or impaired glucose intolerance, is a common kind of diabetes that affects 14 percent of pregnant women, or 135,000 women per year in the United States, and is a risk factor for DBT-2 in moms. Due to differences in ethnicity, selection criteria, and GDM and DBT-2 testing, the stated risk varies in magnitude. Respiratory distress syndrome, neonatal hypoglycemia, and foetal macrosomia can all be symptoms of gestational diabetes. Birth trauma, shoulder dystocia, and caesarean delivery are all more common in newborns. Glycemic management is now recommended as an approach for reducing these maternal and foetal problems, according to new guidelines. The majority of women with gestational diabetes can regulate their blood sugar with diet and

exercise, but others will need to take oral diabetes medication or insulin (Jovanovic et al., 2001).

Catamenial Hyperglycaemia

Diabetic ketoacidosis (DKA) is a condition that can occur as a result of infection, insufficient insulin or poor insulin compliance, acute pancreatitis, stroke, medications, metabolic abnormalities in the body, or treatment neglect (Coustan et al., 1995). Catamenial diabetic ketoacidosis or catamenial hyperglycemia is uncontrolled hyperglycemia with DKA that occurs before the menstrual cycle in females. Uncontrolled hyperglycemia resulted in a fourfold increase in insulin demand. Even with continuous insulin infusion, the condition worsens, culminating in vomiting and severe acidosis, ketonuria, and hyperglycemia. Even inflammatory markers, blood count, renal function, ECG and chest radiograph, thyroid function, and urine and blood cultures were all found to be normal, which was strange. The causes of catamenial hyperglycemia have yet to be identified (Kronenberg et al., 2008). Hormonal changes that occur during the menstrual cycle, as well as dietary and activity modifications may all play a role. The right pharmacological strategy for treating catamenial diabetic ketoacidosis and avoiding diabetic emergencies will be an effective diet and activity plan that includes an increased insulin infusion dosage (Ovalle et al., 2008, Buse et al., 1998, Mohan et al., 2013).

Diagnosis criteria for DBT-1

The measurement of fasting blood glucose concentration has been used to diagnose diabetes mellitus (DM) for many years. DM can be diagnosed if the fasting plasma glucose (FPG) is greater than 126 mg/dl and the random blood glucose concentration during the glucose tolerance test is greater than 200 mg/dl3 in the context of clinical symptoms. ` Professional organisations, such as the American Diabetes Association (ADA), have lately advocated that a glycated haemoglobin (HbA1C) concentration of more than 48 mmol/mol be used to diagnose diabetes (6.5 percent). HbA1C is a regularly used chronic glycemia marker that measures non-enzymatic glycation of haemoglobin and represents average blood glucose levels over a period of two to three months.

It can be used to diagnose DM if the threshold is greater than 6.5 percent (which corresponds to a blood glucose level of 140 mg/dl). The HbA1C test should be carried out using a method that is NGSP-certified and standardised according to the DCCT. Furthermore, while lower C-peptide concentration as a marker of seen endogenous insulin deficiency is useful in guiding both treatment and classification in cases of DM assessed more than three years after clinical diagnosis, no single

clinical feature can perfectly distinguish DBT-1 from non-type DBT-1 at diagnosis. Classification is based on an understanding of various risk factors for type DBT-1 vs. other subtypes, as well as the integration of clinical aspects like as age of diagnosis, BMI, and biomarkers such as pancreatic autoantibodies (Inzucchi et al., 2002).

Antibodies against certain -cell proteins such as insulin islet antigen-2, glutamate decarboxylase, zinc transporter 8, and tetraspanin-7 are found in 90% of those newly diagnosed with DBT-1. India is the world's diabetes capital, according to physicians, who attribute the disease's spread to our increasingly sedentary lifestyle, poor eating habits, and lifestyle choices such as smoking and drinking. However, we know that India has a method for treating this ailment that is free of all the side effects associated with allopathic drugs (Chakrabarti et al., 2002, Meglio et al., 2018).

Symptoms of DBT-1

Diabetes is caused by a lack of physical labour, intense mental strain and stress, a flawed lifestyle, and incorrect food habits, to name a few. The amount of insulin generated by the pancreas is reduced quantitatively in diabetes, resulting in an increase in blood sugar levels and the excretion of excess sugar through urine. Modern medical science considers diabetes to be a lifelong illness, although it can be treated and managed with changes in lifestyle and food, as well as Alternative Medicine such as Yoga, Naturopathy, Ayurveda, Homeopathy, and Unani and Home Remedy (Kahanovitz et al., 2017).

Others symptoms of DBT-1

Urine that is sticky and concentrated is an indication of diabetes, as is frequent urination caused by high glucose. Hunger is caused by the body's production of insulin in response to high blood sugar levels, which promotes hunger. Thirst that refuses to go gone Skin becomes infected as it dries up. High blood pressure causes glucose absorption, which causes changes in the lenses of the eyes. Tiredness and weakness are caused by high blood pressure and an irregular delivery of sugar to the brain and other body organs. The normal functioning of White Blood Corpuscles is hampered by high blood sugar, which causes wound healing to be delayed (WBC), Itching, and Changes in lipid and protein metabolism, as well as burning of the palms and soles, might induce weight fluctuation. Other symptoms include drowsiness and a lack of sexual drive (Chakrabarti et al., 2002).

Complications of diabetes disease

Diabetic patients of type 1 (DPT-1) are increasing at a rate of 2% to 3% per year all over the world. DBT-1 instances are most common in children under the age of

15 years. The previous causes of diabetes type-1(DBT-1) which are genetic mutations, implicating behavioural or environmental influences both, are not validated. Obesity is a common problem among youngsters in modern times. Obesity can impact the beta cell because it puts more pressure on them and reduces their sensitivity, which can lead to a reduction in insulin production. One of the reasons for DBT-1 sickness in young children is because of this. However, this varies from country to country. Higher blood glucose levels, polyuria (increased urine), polydipsia (increased thirst), polyphagia (increased appetite), weight loss, and exhaustion are all common signs and symptoms of DBT-1 disease. It's a chronic endocrine issue, as well as a T-cell-related autoimmune disease. Both issues accelerated the damage to pancreatic -cells over time. It is the primary cause of insulin insufficiency, which results in elevated blood glucose levels, hyperglycemia, and ketoacidosis (Meglio et al., 2018).

Type DBT-1 is a common autoimmune condition. It's linked to an IgG autoimmune illness that causes autoantibodies [glutamic acid decarboxylase antibodies GAD] to attack pancreatic -cells, increasing their demise. Furthermore, type DBT-1 is linked to more than only genetic factors. Environmental factors also play a role. Water pollution, biological life cycle, and nutrition-related difficulties such as vitamin D insufficiency, cow's milk proteins, gluten, newborn and adult diet, and pancreatic poisons such as streptozotocin and nitrites; psychological variables; and virus infection factors are all linked to producing DBT-1 disease.

Viruses, such as rubella virus, rotavirus, mumps virus, cytomegalovirus, and enteroviruses, are among the most likely environmental contributors in the development of T1DM.

Entero-viruses appear to be the most viable candidates for viral triggers with clinically significant connections with T1DM development, according to recent investigations utilising various techniques. Patients with DBT-1 have a higher risk of microvascular complications such as nephropathy, retinopathy, and neuropathy, as well as macrovascular complications such as myocardial infarction, cerebrovascular accident, cardiovascular disease-related death, and all-cause mortality when compared to the general population. According to several observational studies, lowering blood glucose levels in patients with DBT-1 is linked to a lower risk of vascular problems (Mo et al., 2014, Kurkela et al., 2021).

CAUSES OF DIABETES

Age: > 80% of cases occur after 50 years, with the risk of a significant increase after 65 years, Hereditary & Genetics:

Some genes are passed on from parents to their children, Age: > 80% of cases occur after 50 years, with the risk of a significant increase after 65 years, Nutritional Deficiency: Diabetes is caused by poor nutrition, low protein and fibre intake, and a high intake of refined goods. Obesity and fat distribution, overeating, and a sedentary lifestyle are all linked to a higher risk of diabetes. Drugs like steroids, Dilantin, alloxan, streptozocin, and thiazide diuretics are known to promote diabetes, and stress, tension, and worry are cited as the disease's precursors. Down's and Turner's syndromes can result in lifelong diabetes. The pancreas is affected by virus infection, such as Strephylococci. Males in their forties and fifties are more likely to have numerous pregnancies, as are females with multiple pregnancies. Hypertension/High Blood Pressure and Diabetes have a tight association. a higher level of cholesterol, Excessive consumption of oil and sugar, as well as a high-carbohydrate and high-fat diet High blood pressure and surgery to remove the pancreas (Kurkela et al., 2021).

DIAGNOSIS OF DIABETES

Fasting Plasma Glucose (FPG) Test: This test is used to check for pre-diabetes and diabetes in patients who have asked not to eat for 8 hours. When done first thing in the morning, it's the most reliable. The Oral Glucose Tolerance Test (OGTT) is used to detect diabetes and pre-diabetes by measuring blood glucose levels after an 8-hour fast and 2 hours of glucose consumption. A blood glucose result of 200 mg/dL or greater indicates diabetes in a random plasma glucose test. Fingerstick Blood Glucose: A simple blood glucose test that may be done anywhere. Glycosylated Hemoglobin Test: This test is used to monitor elevated blood sugar levels for up to 120 days (Verhulst et al., 2019, Ludwig et al., 2002).

Physical Examination

Urine sugar, urine ketone, and C-peptide blood tests are all available.

Complications of DBT-1

Increased blood sugar causes narrowing of blood arteries, which can lead to a heart attack or stroke. Kidney Disorders: High blood sugar causes the kidney to work harder, causing it to malfunction. Erectile Dysfunction and Hypoglycemia (Low Blood Glucose), Sexual and Urologic Problems, Stomach Nerve Damage (Gastroparesis), Eye diseases: diabetes narrows the retinal vein and causes Cataracts, Retinopathy, and Glaucoma, Bone and Joint disorders, Skin problems, digestive problems, and tooth and gum problems, Infections: High blood sugar weakens the immune system, making it vulnerable to a variety of infections, as well as nerve damage (neuropathy), dental problems, skin and foot disease, and diabetic coma.

TREATMENT AND MANAGEMENT OF DBT-2 AND DBT-1

Anthocyanidins, Anthocyanins, Flavones, Isoflavones, Flavan-3-ols, Isoflavonoids, Chalcones, Tannins, Xanthones, Organic acids, Cinamic acid derivatives, Sugars, Curcuminoids, and Alkaloids, among others, have been identified as possible antidiabetic bioactive components. Furthermore, these substances are -glucosidase inhibitors. All of these bioactive substances are now being used to treat diabetes. Many therapies have been employed to treat and manage disease, some of which are listed here (Tyagi et al., 2014).

Ayurvedic Cure for DBT-1

The Ayurvedic treatment is more effective and important in curing diabetes. Type 1 diabetes and DBT-2 can be cured with Ayurvedic diabetic medicine and herbs. Ayurvedic components and mixtures aid in the treatment of the condition are following

1. Bitter gourd, Rose apple, Bel, and Neem juice can be taken on an empty stomach every day. It is the most effective diabetes treatment.

2. Turmeric is also an effective treatment for it.

3. Take mixture of 1/2 teaspoon ground bay leaf, 1/2 teaspoon turmeric and 1 teaspoon aloe vera gel, twice a day before lunch and dinner to control blood sugar.

4. A natural remedy for diabetes patients is to take mixture of 100 gm grind seeds of Methi, Turmeric 50gm and white pepper with a glass of milk twice a day.

5. Mixture of Amalaki Churna (500mg), Turmeric Powder (500mg) and Naag Bhasma (125mg) with honey can help lower blood sugar and improve pancreatic function.

6. On an empty stomach, drink a glass of water with extract of 10 Tulsi leave, 10 Neem leaves and 10 Belpatras, to lower blood sugar levels.

7. Drinking copper vessel water in the morning is also beneficial.

8. Bel leaves have anti-diabetic properties; combine its extract with black pepper.

9. Garlic contains allicin, which lowers blood sugar levels and aids in the breakdown of cholesterol.

10. Jamun leaves have the ability to control the conversion of starch into sugar and are an excellent Ayurvedic treatment for the disorder.

11. Onion has low sugar content.

12. Other diabetes-friendly herbs include Jambhul, Gurmar, Sagar got, Shilájit, Triphala, Gurmar Leaves, Nayantara, and Sagar gota.

13. Take 14-28 mL of bel leaf juice with 5 to 10 gm of honey three times a day. It is an effective treatment for DBT-2.

14. Take 12 gm bastard flower powder with 5 to 10 gm raw sugar three times a day. It aids in the reduction of blood sugar levels.

15. 14 to 28 ml of embolic myrobalan fruit juice and the same amount of turmeric juice to be taken three times a day for a positive result.

16. Powder of Indian Sarsaparilla stem (1 part), Tamala leaf (1 part), and root of glycyrrhiza (1 part) to be taken twice a day in 1 gm dose with 50 to 100 ml water for cure of diabetes.

17. A 14 to 28 ml decoction of equal parts white acacia bark, khair, and areca nut, to be taken three times a day aslo improves the diabetic condition (Sodhi et al., 2014).

Common list herbal drugs are shown below which are using for the treatment and management of diabetic disease.

Table.1 List of anti-diabetic medicinal plants with bioactive compounds activity (Dubey et al., 2021)

Parts of plant	Bioactive compounds
Gallega officinalis leaves, seeds	galegine
Syzygium cumini seeds, leaves, flower	mycaminose
Bauhinia forficate leaves, flowers,	kaempferol-3-neohesperidoside (insulin mimetic)
Bidens pilosa L. whole plant	polyacetylenic glucosides
Swertia punicea whole plant	methylswertianin, bellidifolin
Capparis moon fruits	gallotannins (chebulinic acid derivatives)
Artemisia dracunculus L. whole plant	davidigenin, sakuranetin, 2',4'-dihydroxy-4-methoxydihydrochalcone, 4,5-di-O-caffeoylquinic acid, 5-O-caffeoylquinic acid, 6-demethoxycapillarisin
Salacia reticulate root, stem	Salacinol, kotalanol, de-O-sulfated salacinol, de-O-sulfated kotalanol, ponkolanol, salaprinol
Morus alba leaves	quercetin 3-(6-malonylglucoside), rutin (quercetin 3-rutinoside), isoquercitrin (quercetin 3-glucoside)

Plant	Bioactive molecules
Ocimum sanctum leaves	polyphenols, caffeic acid, p-coumaric acid
Acacia pennata shoot tips	polyphenols, caffeic acid
Solanum xanthocarpum fruit	polyphenols, caffeic acid
Macaranga tanarius seeds	ellagitannins (mallotinic acid, corilagin, chebulagic acid, macatannins A and B)
Eleutherine Americana bulb	eleutherinoside A
Aquilaria sinensis leaves	mangiferin, iriflophenone 2-*O*-α-L-rhamnopyranoside, iriflophenone 3-*C*-β-D-glucoside, iriflophenone 3,5-*C*-β-D-diglucopyranoside
Panax japonicas root	polyacetylenes, phenolic compounds, one sesquiterpenoid, one sterol glucoside
Curcuma longa hizome	curcumin, demethoxycurcumin, bisdemethoxycurcumin, ar-turmerone
Rhododendron tomentosum Picea mariana fruit	quercetin
Aronia melanocarpa fruit	anthocyanins
Stevia rebaudiana leaves	alkaloids, flavonoids
Nigella sativa seeds	gallic acid, (–)-*p*-hydroxybenzoic acid, chlorogenic acid, vanillic acid, *p*-coumaric, ferulic acid, *trans*-2-hydroxycinnamic acid, *trans*-cinnamic acid, epicatechin, (+)-catechin, quercetin, apigenin, amentoflavone, flavone
Phaseolus vulgaris L. seeds	alkaloids, flavonoids, fiber, proteins, tannins, terpenoids, saponins, quercetin, anthocyanin, catechin
Marrubium vulgare aerial part	flavonoids
Ruta graveolens leaves	rutin
Carissa carandas fruit	gallic acid, flavonoids
Pinus pinaster bark	polyphenols: proanthocyanidins, catechin, epicatechin
Piper retrofractum fruits	piperidine alkaloids: piperine, pipernonaline,dehydropipernonaline
Withania somnifera leaf , Root	withanolides
Trigonella foenum-graecum (Fenugreek) seeds	saponins, coumarin, fenugreekine, nicotinic acid, phytic acid, scopoletin and trigonelline.
Tinospora cordifolia whole plant	Alkaloids, Terpenoids, Lignans, Steroids and others
T. arjuna bark	E- llagic Acid B-sitosterol.
Terminaliachebula fruits	Chebulic Acid chebulogic Acid gallic acid
Terminalia bellerica fruits extracts	phenols, flavonoids, alkaloids, terpenoids, saponins and glycosides
Moringa oleifera pods	quercetin and kaempferol
Syzygium cumini bark	Triterpenes/steroids, glycosides, carbohydrates, alkaloids, flavonoids, saponins, tannins and amino acids.
Swertia cordata and Swertia chirayita (Gentianaceae) Whole part	Gentiopcrin
Stevia rebaudiana	Hydrocarbons & Diterpenes, glucosides Stevioside, Rebaudioside Dulcoside, Rebaudioside
rhizomes of Polygala senega L	Hydroxycinnamin acid, arabinose, melibiose, 1,5- anhydro-D glucitol.
Semecarpus anacardium (Linn.) bark	Biflavonoides, Phenolic bhilawanols, minerals Vitamins, Amino Acid Anacardosidc.
Sage (Salvia officinalis L.)	5-methoxysalvigenin, camasol, 1, 8-cineole, linalyl acetate.
Putranjiva roxburghii Wall barks	terpenoids, mustard oils, flavonoids, tannins, alkaloids, glycosides and phenolic compounds
Pterocarpus Marsupinum heart wood	Kinotannic Acid kinored K-Pyrocotechin (Catechol) Resin, gallicacid.
Picrorrhiza kurroa Rhizomes	Picroside-I , Picroside-II, kutkiside.
Phyllanthus Amarus Whole plant	Lignans-a diarulbutane Phyllanthin Hypophyllanthin Amariin, Amarulone.
Urtica dioica Leaves	Carbonic, isorhamnetin, kaempferol, quercetin.
Murraya koenigii Fresh, green, mature curry leaves	Pyroanocarbazole type aldaloid myrrayacine
Momordica charantia fruit	Triterpenoid, Saponins Charantin, momordicin.
Mesua ferrea flowers	Betulinic Acid. 1,8 dinydroxy-3methoxy6- methul anthraquinone, Hydrocarbons, Carboxylic Acid.
Althaea officinalis	Arabinas, glucans, arabinogalactans,isoscutellarin, ferulic, syringin.
Juniper "berries	Diterpene acids, ascprbic acid, glucurosnic acid,
Java tea	Orthochromene, methylripariochromene, acetovanillochromene, Dieterpenes, ß-elemene, β-caryophyllene.
Ispaghula seeds	Boschniakine, boschinakinic acid, aucubin, placteose, priterpine.

Hybanthus enneaspermus whole plant	alkaloids, dipeptide, isoarborinol, sitosterol, flavonoids, sugars, tannins
Panax ginseng berry	Protopanaxadiol, protopanaxatriol, panacene, limonene, terpineol.
Ginger dried rhizome	Starch, palmitic acid, oleic acid, linolenic acid, caprylic acid, arachidic cid, zingerone, zindiberol.
Garlic bulb	Allinase, peroxidase, myrosinase, aliyipropyl disulfide, ajoene, s-allylmercapotcysteine.
Feniculam Valgare leaves	Fenchone, Anethole Phellandrene Lemonene
Evolvulus alsinoides whole plant	Shankhpushpine Volatile oil
Eugenia jambolana seed, kernel, and seed coat	isoquercetin, kaempferol
Eucalyptus leaf	Citronellal, citronellol B-pinene, p-cymene cineole, linallol.
Emblia ribes berries	embelin, volatile oil, fixed oil, resin, tannin, christembine (alkaloid), phenolic acids like caffeic acid, vanillic acid, chrorogenic acid, cinnamic acid, o-cumaric acid. 4.33%
Embelica officinalis seeds	Vitamine, phyllemblin tannins.
Dandelion leaf and root	Cichoric acid, aesculin, lueteolin-7-diglucoside, oieic acid, onocafferyl tartaric acid
Turnera diffusa (damiana) leaves and stems	Tetraphyline B, calamine, 1-8-cineole,B-copaene, arbutin.
Commiphoramyrrha gum resin	Sesquiterpenes & Acid a pinene, cadinene Limonene, Eugenol, Cuminaldhyde, Acetic Acid, m-cresol.
Cinnamon Zeylanicum bark	Poly-phenol, Eugenol, Cinnamaldehyde Phellandrene, Pinene, Cymene, Caryolonyllenq.
Centella asiatica whole plant	Asiaticoside madecassoside.
Apium graveolen L. (Celery seeds)	Apiginin, apigravin, celerin, B-eudesmol, myristic, rutaretin.
Capparis deciduas, flowers, fruits, stems, seed and leaves	amino acids, sterols, tocopherols, phenols
Arctium lappa (burdock), (A. lappa) root	Fukinone, B-setolone, resin, B-inesmol, myristic, rutaretin.
Bombax cieba bark extract	Lupeol, a sitosterol sesquiterpenes Flovonoid Alkaloids, steroids Caleium & Napthaquinones.
Boehavia diffusa or (Punarnava) leaf	Punarnavine Punernavoside.
Blueberry fruits	Anthocyanin, Caffeoylquinic 3,5 dicafeylqunic neo chloroqnic 4 caffcoyl quinic 3coumaroulqunic Chloroqenic Acid.
Bhumi Amla or Phyllanthus Amarus leaves	Lignans-a diarulbutane Phyllanthin Hypophyllanthin Amariin, Amarulone.
Azadirachta Indica leaves	Azadirachtin Meliantriol Nimbin, Nimbidin, Myricitin.
Andrographis- Paniculat whole part	Androgrpholide
Amaranthus spinosus leaves	amaranthoside, a lignan glycoside amaricin, a coumaryl adenosine along with stigmasterol glycoside, betaine, such as glycine betaine and trigonelline
Aloe vera juice leaves	Pentocides-Barbaloin, aloin, isobarbaloin, betabarbaloin
Fresh and recently cropped Allium cepa	Organic acids profile (malic, citric, succinic, pyruvic, oxalic, ascorbic, and tartaric acids) highlighted malic and citric acids in higher amounts in all landraces. Fructose, glucose, and sucrose
Alfalfa whole part	Malonic acid, trigonellinge, arginine, medicagol, genistein, campesterol, B-carotene
Alangium lamarckii leaves	alkaloids, deoxytubulosine, alangimarckine, dehydroprotoemetine, phenolic glycosides, salviifosides A-C, salicin, kaempferol, and kaempferol 3-O-b-D-glucopyranoside
Ailanthus excelsa leaves	Phytol, linolenic Acid, Flavonoids, Saponins, Protein, Quassinoids, terpenoids, Cumarins
Agrimony	Apiginin, lutiolin, ellagitannin, Quercitrin, ursolic acid.
Aegle marmelos leaf	Marimelosin Furocumarin
dhatoda zeylanica leaves and twigs	pyrroloquinoline alkaloids such as vasicine, vasicol, adhatodine, vasicinone, vasicinol, vasicinolone
Acacia-or Acacia Arabica bark	Arabin oxidase

Amazing bioactive compounds having remedies for DBT-1

1. Remedy at home with the bitter gourd is the most important in diabetes management. It has hypoglycaemic action, which helps to treat both DBT-2 and DBT-1. The best treatment is to drink half a cup of juice first thing in the morning.

2. Bengal gramme (Chana) is effective in the treatment of chronic diabetes. In terms of glucose tolerance and urine excretion, it performs well.

3. Including bitter melon in one's regular diet can help diabetic patients control their blood sugar levels.

4. Drinking 1 cup of fenugreek (Methi) juice first thing in the morning on an empty stomach lowers blood glucose levels. In diabetic individuals, it lowers reactive hyperglycemia, glucose, serum cholesterol, and triglycerides.

5. Vitamin C is present in Indian gooseberry and orange, which is useful to diabetic patients.

6. The juice of Indian gooseberry and bitter gourd stimulates pancreatic cells to release insulin and lower blood glucose levels (Shukla et al., 1973, Tyagi et al., 2014, Bhattacharya et al., 2009).

7. Mango leaves in 1 glass of water, left overnight to lower blood glucose levels, filtered and consumed.

8. Grapefruit is an excellent food for diabetic patients.

9. Eating curry leaves twice a day helps to lower blood sugar levels.

10. Take roughly 12 tsp of each ground bay leaf + turmeric + aloe vera gel before lunch and dinner to lower blood glucose levels.

11. The combination of honey, turmeric powder, and dried gooseberry powder lowers blood sugar levels.

12. Diabetic individuals can use a home cure for diabetes by chewing 4-5 Jambul fruit (Jamun) leaves in the morning and evening.

13. Chewing two Neem and Bilva leaves each has a significant impact on controlling this problem.

14. Eating soaked almonds overnight can also help to heal diabetes.

15. Basil leaves, neem leaves, Belpatras leaves, and 1 glass of water will help lower blood sugar levels.

16. Apple juice has been shown to be useful to diabetic people.

17. Including garlic, karela, onion, and soybean in your daily diet can help you lower your blood sugar.

18. Drinking more water in the morning or before exercising helps to lower blood sugar levels.

19. Fresh Margosa leaf juice can aid with diabetic management.

20. In such a situation, string bean pod tea is an effective natural insulin alternative.

Diabetes Diet Plan

A diabetic patient's diet is extremely important. The purpose of a diabetic diet is to avoid blood glucose spikes by eating properly and maintaining an appropriate body weight. The patients' food regimen should consist of three meals and three snacks. The fundamental goal of a diabetic diet is to keep blood sugar levels between 70 and 140 mg/dl, cholesterol levels between 200 mg/dl, and blood pressure between 120 and 80 mm Hg. The following is a diet plan for such a patient:

1. Morning: 1-2 ounces bitter gourd juice (40 ml)

2. Breakfast: 250-400ml skimmed milk or butter milk, or 50 gm sprouted gramme, moong, or methi, or 50 ml fresh amla juice

3. Lunch: 25-50 g roti (wheat + gramme flour), 250 g green veggies, 50 g salad, 25 g moong 150g curd + 1 glass buttermilk

4. In the evening: 30 gm roasted gramme, vegetable soup, or 1 glass butter milk

5. Dinner: Same as lunch, however curd is not recommended at night.

6. Diabetes-Friendly Fruits

The following are some of the most beneficial foods for diabetes individuals. Some foods should also be avoided since they have been linked to heart disease and high blood pressure:

1. Fibrous fresh fruits and vegetables are beneficial.

2. Soybean, bean, turnip, cucumber, garlic, Lauki, Bitter gourd, Spinach, Fenugreek, Bathua, Chaukie, Amla, Jamun, Bel, cabbage, tomato, and carrot (Singh et al., 1997, Baldwa et al., 1977).

Bioactive compounds having homeopathic medicine for DBT-1

Homoeopathy plays an important role in the treatment and management of diabetic patients. Hyperglycemia can be effectively treated with following homoeopathy measures.

1. Phosphorus keeps the blood sugar levels stable.

2. Syzygium Jambolanum immediately lowers blood sugar levels; It is generally used in dose of 5 drops in every 6 hours.

3. Aurum Metallicum reduces patients' sugar cravings.

4. Uranium Nitricum relieves nephrotic symptoms.

5. Arsenicum Bromatum normalises the disorder's excessive thrust and hunger.

6. Insulin: aids in the proper functioning of the pancreas.

7. Phosphoric acid has a remarkable ability to treat diabetes in its early stages.

8. Lactic acid is an effective treatment for such patients (Singh et al., 1997, Baldwa et al., 1977).

Bioactive compounds having unani system for DBT-1

The Unani System believes that stimulating the pancreatic cells is the only way to completely heal diabetes mellitus. The pancreas is restored and rejuvenated by preparations such as black pepper oil, fennel, and juniper. Carrot, eucalyptus, fennel, geranium, and lemon oils all have an insulin stimulating effect.

Naturopathy for DBT-1

Diabetes mellitus is a nutritional condition marked by high blood glucose levels and the presence of glucose in the urine. DBT-1and DBT-2 is caused by anomalies in glucose, protein, and lipid metabolism caused by a lack of insulin. Nature has the ability to treat diabetes completely as soon as possible.

Yoga therapy for treatment and management of DBT-1

Yoga is an excellent remedy for diabetes management. Yoga therapy for hyperglycaemia is perceived to be rapid in the early stages and significantly useful after continued practise. Yogic practises assist in the restoring normal function of afflicted pancreas and compensate for the lack of insulin secretion. Yogic treatment lowers blood sugar levels considerably. In addition, glucose tolerance improves. Yoga enhances one's psychological makeup as well as one's overall sense of well-being. Within 6 weeks, yogic treatment may be able to regulate diabetes (Inayat-ur-Rahman et al., 2009, Balaji et al., 2011).

The following practices of Yoga are quite effective for DBT-1and DBT-2 mellitus:

1. Sirsasana (Headstand pose) revitalises the nerve system and pituitary gland, which are both involved in sugar regulation. As a result, there is a considerable and good influence in the alleviation of the diabetes.

2. Paschimotasana (Powerful pose) strengthens the pancreas, spleen, and kidneys. This Yoga pose aids in the treatment of diabetes mellitus.

3. Veerasana (Hero's pose) promotes physical and mental stability, which alleviates tiredness and weakness.

4. Dhanurasana (Bow pose) stimulates the pancreas, causing it to secrete the appropriate amount of glucagon and insulin at the appropriate time, making it an effective treatment for the disorder.

5. Diabetes is also helped by Shalabhasana (Locust Pose).

6. Katichakrasana (waist rotating pose) helps to lower blood sugar levels and provides a wonderful sense of lightness.

7. Ardha matsyendrasana (Half spinal twist poses) alleviates diabetes by lowering blood sugar levels.

8. Mayurasana (Peacock Asana): People with diabetes benefit from this asana because it strongly stimulates the metabolic process.

9. Bhujangasana (Cobra pose) stimulates the pancreas and aids in insulin secretion.

10. Uddiyan Bandha is beneficial to the overall functioning of the hormonal glands.

11. Bhastrika Pranayama (Bellows Pranayama) helps in digestion and enhances overall body function.

12. Naddishuddhi Pranayama is also beneficial in diabetes

13. Surya Nmaskar (Sun Salutation) is also suggested to treat the disorder.

14. Relaxation techniques such as Shavasana, Makrasana, and Balasana are extremely beneficial for DBT-1.

Foods and diet plan for treatment and management of DBT-1 (Mohan et al., 2013).

Cakes, fast food, jaggery, ghee, butter, cold drinks, biscuits, dried fruits such as badam, and cooking oil

Diabetes can be controlled and managed to a greater extent with the support of a regulated diet, an alternative medical system, and a good exercise module:

1. Completely avoid sugary substances/products.

2. Junk food, fatty, fried, and fat-rich foods should be avoided at all costs.

3. Foods that are high in fibre should be preferred.

4. Stay away from non-vegetarian foods.

5. Ghee, Vanaspati, fine flour, smoking, and chewing Jarda and Gutka are all to be avoided.

6. Stay away from stress because it is the source of many disorders.

7. Excessive and frequent eating puts your health at jeopardy.

8. Your indifference to exercise could put you in risk.

9. Combine healthy physical activity with Yoga and meditation.

10. Diabetic Way of Life (Ayurveda Diabetes Treatment).

11. Don't sleep during the day.

12. Stay away from alcoholic beverages.

13. Don't smoke.

14. Look after your ENT system.

15. Exercise on a regular basis.

16. Practice yoga.

17. Take extra precautions with your food.

18. Create a nutritional plan.

2. Diabetes Kinds based on Insulin Insufficiency Diabetes can be categorised into the following types based on insulin deficiency.

Other therapies for treatment and management of DBT-1

In hyperglycemic individuals, mud therapy has been shown to be effective.

Treatment using water, known as hydrotherapy, is an ancient method of treating high blood glucose levels. Wet abdomen pack, spinal bath, hot and cold fomentation over abdomen, cold hip bath, hot and cold hip bath, wet abdomen pack all of these are crucial components of treatment. The colon was thoroughly cleansed, and the enema assisted the intestine in resuming its typical features.

Cold water bathing enhances blood circulation and encourages muscle glucose utilisation. Massage therapy helps diabetic individuals lower their blood sugar levels by invigorating and rejuvenating the entire body.

Sun Bath: Half cup of water stored in a brown container and exposed to sun rays for at least 8 hours, dosed twice a day after meals, has also been found to be effective. Diabetic patients can benefit from daily exercise, particularly morning walks.

MODERN TECHNOLOGIES AND DBT-1 AND DBT-2

The application of nanotechnology to the treatment of diabetes has resulted in innovative glucose monitoring and insulin delivery systems. The benefits of glucose sensors and closed-loop insulin administration techniques in facilitating diabetes treatment have been established by researchers to be advantageous in both DBT-1and DBT-2 (Inayat-ur-Rahman et al., 2014).

Nanotechnology and Diabetes

A nanomedical device is a microcapsule with pores that has shown to be a potential method in drug delivery. These holes are large enough to let small molecules like oxygen, glucose, and insulin to pass through, but small enough to allow larger immune system molecules like immunoglobulins and graft-borne virus particles to pass through. Replacement islets of Langerhans cells, largely produced from pigs, could be implanted beneath the skin of diabetic patients in microcapsules. This could re-establish the body's sensitive glucose control feedback loop without the use of potent immunosuppressants, which can put the patient at danger of infection. (Balaji et al., 2011, Patwardhan et al., 2004) Table 2 outlines the major issues surrounding diabetes and the role of nanomedicine in its therapy. The nanoparticle targeted drug delivery strategy offers numerous advantages, including increased drug bioavailability by targeting specific tissues, organs, and tumours and delivering the maximum dose of drug directly to the target spot. The scalability of a nanoparticle is one of the most difficult technological hurdles. Manufacturing three-dimensional nanostructures, as opposed to stand-alone or two-dimensional layer-shaped nanosurfaces, is a difficult operation due to the lack of standardised manufacturing procedures. Another concern is that nanoparticle exposure could be harmful or dangerous. Concerns regarding the harmful effects of manufactured nanomaterials like carbon buckyballs and nanotubes when inhaled, eaten, or absorbed via the skin are growing. (Balaji et al., 2011) Insulin is required for DBT-1and DBT-2, and earlier insulin delivery systems were plagued by infections, painful administration, and poor patient compliance. Recent micro- and nanotechnologies, on the other hand, have made insulin administration easier by allowing for the modulation of insulin delivery, which includes pulmonary, nasal, transdermal, and closed-loop delivery. (Shah et al., 2012, Gæde et al., 2003, Chen et al., 2012, Buse et al., 2003).

A New Look at Statin Therapy

Statins are inhibitors of 3-hydroxy-3-methylglutaryl coenzyme A, which block a critical process in the liver that lowers LDL cholesterol levels in the blood. Statin therapy lowers low-density lipoprotein (LDL) cholesterol to a significant level, lowering the risk of coronary artery disease significantly [41-42]. Diabetes guidelines from the National Institute for Health and Clinical Excellence (NICE) and the Scottish Intercollegiate Guidelines Network (SIGN) recommended lipid-lowering therapy as primary prevention (when used regularly) for patients

with DBT-2 over 40 (Grade A recommendation), as well as consideration for patients with DBT-1over 40 (Grade B recommendation) (Grade B recommendation) (Drummond et al., 2010). According to data presented at the European Association for the Study of Diabetes meeting in Stockholm, statin medication is being examined and used less in patients with DBT-2 in a large American sample of over 100,000 people (Radican et al., 2010). Statins have a high efficacy and are useful in lowering cardiovascular events in patients with low cholesterol levels and no heart disease. HMG-CoA reductase inhibitors or statin therapy, on the other hand, have some drawbacks. Renal failure, muscular diseases ranging from myositis to full rhabdomyolysis, and hepatic dysfunction are all unusual adverse effects that can be handled by the patient (Jukema et al., 2012).

A Novel Therapeutic Approach

Modern using Stem Cell Technology The hunt for a prospective diabetes treatment has led to the exploration of a number of new scientific fields, one of which is stem cell technology. DBT-1and DBT-2 diabetes both are known to be caused by a lack of cells in the pancreatic cells, resulting in inadequate insulin secretion. The techniques should either try to correct abnormalities in pancreatic cells or to improve the sensitivity of body cells to insulin action. Current efforts aimed at islet cell and pancreas transplantation are limited due to a paucity of donor organs, whereas cell replacement strategies offer a unique source (Meier et al., 2006). DBT-2, in contrast to DBT-1and DBT-2, which is characterised by autoimmune destruction of pancreatic cells, is caused by abnormal cell activity along with insulin resistance in peripheral organs (Butler et al., 2003). Because of its immunosuppressive character, mesenchymal stem cell (MSC) therapy has emerged as a viable therapy in the treatment of DBT-1. Due to direct contact and the formation of soluble indicators, MSCs have been reported to have immunomodulatory effects both *in-vitro* and *in-vivo* (Abdi et al., 2008, Spaggiari et al., 2009, Wu et al., 2008, Tyndall et al., 2007). MSCs have the ability to develop into several different types of mesenchymal cells. Hematopoietic stem cells are multipotent stem cells that can give rise to all types of blood cells and also have immunomodulatory properties. As a result, hematopoietic stem cell transplantation has proven to be a viable treatment, with improved cell function in newly diagnosed DBT-1patients (Voltarelli et al., 2007). Further research has shown that DBT-1patients can develop induced pluripotent stem (iPS) cells by reprogramming their adult fibroblasts with three transcription factors (OCT4, SOX2, and KLF4). Diabetes-induced pluripotent stem cells (DiPS) are pluripotent stem cells with the ability to develop into insulin-producing cells. This is advantageous in the modelling of type 1 illness and cell replacement therapy (Maehr et al., 2006).

In vitro and in vivo investigations have revealed that bone marrow-derived MSCs can develop into insulin-producing cells (Tang et al., 2004, Ianus et al., 2003, Ghannam et al., 2010). Because of their pluripotent nature and large-scale generation of different cell lineages in cultures, human embryonic stem cells (ESCs) have drawn a lot of attention in the treatment of diabetes. The study has a number of drawbacks, including a lack of dependable methods for creating specific cell types, immunological rejection of transplanted cells, and difficulty purifying specific lineages (Chien et al., 2004). Concerns also exist about the uncontrolled multiplication of transplanted embryonic stem cells into a specific type after they have been implanted (Hori et al., 2009). Despite its numerous scientific and ethical constraints, the use of stem cell technology in the treatment of diabetes has enormous potential.

Diabetes Gene Therapy

In the 1970s, a series of investigations led to the cloning and production of insulin in culture cells, a huge breakthrough in medicine, and the use of gene therapy in the treatment of diabetes was suggested as a possible cure. The most significant component of the treatment is controlling blood sugar levels, which also helps to lessen the disease's consequences. Two techniques of gene delivery are used in somatic gene therapy, which involves the body's somatic cells**.** Ex vivo gene therapy is defined as the process of removing tissues from the body, inserting therapeutic genes in vitro, and then reimplanting them back into the body, whereas in vivo gene therapy is defined as the process of injecting gene therapy vectors directly into patients via subcutaneous, intravenous, or intrabronchial routes, or by local injection (Chan et al., 2003). Ex vivo therapy tries to create cells that have the features of cells, such as insulin-producing cells (Zalzman et al., 2003). Cells for transplantation have also been generated using this technique. However, the element of physically removing the tissue from the patient and reimplantation of the genetically modified tissues back into the patient's body (Chan et al., 2003) is a source of concern. Furthermore, DBT-1 is caused by the autoimmune death of insulin-producing pancreatic cells, and islet transplantation has been considered as a therapy option. Insulin gene therapy replaces cell function by creating insulin secretory non-cells that are immune to autoimmune reactions, providing a promising treatment option for type 1 diabetes (Jun et al., 2005). Because it is simpler because the vector containing the desired gene is directly put into

the patient, in vivo gene therapy is the preferred treatment option. However, developing safe (non-toxic to the host) and effective vectors remains a difficult problem for gene therapists. Currently, there are three ways for in vivo therapy: genetic transfer of noninsulin glucose-lowering genes, gene therapy, and gene therapy. Currently, in vivo therapy strategies include the genetic transfer of non-insulin glucose-lowering genes, as well as the application of blood sugar-lowering genes that act as an enhancer of glucose utilisation by the liver or skeletal muscles, as well as an inhibitor of glucose production by the liver (Chan et al., 2003). The transgenic glucokinase, for example, has been discovered to have a glucose-lowering impact in the liver (Morral et al., 2003). It's possible that the Gck gene improves the body's glucose consumption (O'Doherty et al., 1999). The use of glucokinase genetic transfer as an adjuvant therapy in the treatment of diabetes has been reported (Morral et al., 2002). A gene known as "protein targeting to glycogen" (PTG) was employed to convert glucose to glycogen in another strategy to regulate glucose synthesis in the liver (O'Doherty et al., 2000, Newgard et al., 2000). The PTG protein is a member of the glycogen targeting subunits of protein phosphatase-1, which controls glycogen metabolism. Adenoviral-mediated PTG transfer promotes glycogen synthesis in the liver and lowers blood glucose levels in rats, according to rat experiments. This has been proposed as a diabetic treatment strategy. The transfer of genes that respond to glucose and the application of gene therapy to promote cell formation in the liver are two more fields of genetic engineering. The glucose-responsive genes that have been modified to improve the conversion of proinsulin to insulin, as well as those that show expression after modification, respond to blood glucose levels (Dong et al., 2001, Yoon et al., 2002). Because liver cells lack hormones that convert proinsulin to insulin, new proteolytic cleavage sites have been added to the proinsulin molecule, which are recognised by a protease called furin, which is found in various tissue systems, including the liver (Short et al., 1998, Muzzin et al., 1997, Auricchio et al., 2002). The insulin gene can be altered to produce single-chain insulin (Hui et al., 2002) with 20–40% of the action of mature insulin (Lee et al., 2000). In addition, studies have been conducted to induce the production of cell formation in the liver. Delivering islets-specific transcription factors to endocrine cells can trigger the production of cells, (Kojima et al., 2003, Ferber et al., 2000). Insulin production and control remain challenging to regulate and manage due to a lack of knowledge about insulin metabolism (Halban et al., 2001). The strategy aimed at induced cell neogenesis appears to be a viable therapeutic approach for diabetes, as it may provide a remedy for type 1 diabetes autoimmunity.

Nutritional Therapy for Medical Conditions

Many improvements in clinical research have been made in medical nutrition therapy in the prevention and management of diabetes, with the goal of using nutrition therapy to treat ailments and illnesses. The term "medical nutrition therapy" was coined by the American Diabetes Association in 1994, and it consists of two phases: determining a person's nutritional needs and treating them through counselling and nutrition therapy, respectively (Pastors et al., 2002). Nutritional therapy for diabetes aims to maintain an optimal amount of lipids in the blood, an appropriate body weight, and a normal blood glucose level. Nutrition therapy as a diabetes treatment is dependent on a number of factors, including the patient's age-related nutritional needs and food preferences, as well as other medical conditions, as well as an exercise regimen and recommended nutritional requirements based on the patient's abilities and health conditions (Pastors et al., 2002). The proportion of carbohydrate intake is depending on the patient's protein and fat intake, according to contemporary recommendations. A low carbohydrate/high protein diet is popular and may result in weight loss and improved glycemic control in the short term, but it is difficult to sustain over time. Protein should account for 10–20% of total calories, while total fat should be limited at 8%. Natural Products and Diabetes Literature has long advocated for the use of herbal remedies to treat both insulin-dependent and non-insulin-dependent diabetes. Plants with anti-diabetic effects could be used as a supplement to current treatments or as a potential source of novel hypoglycemic chemicals. Naturopathic remedies have been used for a variety of health issues since the dawn of time and are still gaining favour today. Diabetes has been known since the Brahmic period, according to ancient literature, and is mentioned in Ayurvedic literature, such as the Sushruta Samhita, written in the fourth and fifth century BC (Thatte et al., 1989). There are two types of diabetes: one that is inherited and the other that is caused by dietary indiscretion. Herbal medicines are becoming increasingly popular among the general public due to their low cost and lack of adverse effects. Although plant-based medicines have long been used to treat ailments around the world, most of the herbs' mechanisms have yet to be identified and standardised (Prasad et al., 2009). Many new bioactive compounds derived from plants that have hypoglycaemic effects have anti-diabetic action that is comparable to, if not more effective than, recognised oral hypoglycemic medications as daily, tolbutamide, and chlorpropamide. Many other active compounds produced from plants, on the other hand, have not been properly studied (Bnouham et al., 2006). Plants with antidiabetic properties are of particular interest to the ethnobotanical

community (Grover et al., 2002), because they are known to contain valuable medicinal properties in various parts of the world, and a number of them have shown varying degrees of hypoglycemic and antihyperglycemic activity. Many plant species include bioactive components that can be extracted and used as drug lead compounds or pharmacological agents. These tried-and-true methods may hold the secret to resolving diabetes problems (Babu et al., 2006). A Phyto molecule's chemical structure is important for its anti-diabetic effect. (Jung et al., 2018) Certain plant species that are rich in terpenoids, flavonoids, phenolics, coumarins, and other bioactive compounds have been proven to lower blood glucose levels. Several plants, including Allium sativum Linn. (Liliaceae), Gymnema Sylvestre (Retz.) Schult (Asclepiadaceae), Murraya koenigii (L.) Spreng. (Rutaceae), Allium cepa (Liliaceae), Withania somnifera Dunal (Solanaceae), and Ferula foetida Linn. (Umbelliferae Because of its importance in diabetes therapy and control, G. sylvestre's antidiabetic activities have been extensively studied (Tiwari et al., 2014, Sakthivel et al., 2010).

FUTURE PERSPECTIVES

Diabetes has remained one of the most difficult health conditions in the twenty-first century, with a global reach. Diabetes is a severe public health issue, but there is good news: significant progress is being made in diabetes prevention, detection, and treatment. Patients with DBT-1must take insulin 3-4 times a day for the rest of their life, and their blood sugar levels must be monitored on a frequent basis to avoid consequences such as retinopathy and cardiovascular disease risks. Around 1300 patients with DBT-1are anticipated to undergo whole organ (pancreas) transplants and no longer require insulin, however the demand for organ transplantation outnumbers the supply. Rejection of transplanted organs is another risk factor; as a result, the patient is given powerful immunosuppressive medicines, which might lead to additional catastrophic disorders (Sakthivel et al., 2010). Glycemic control must be closely managed in the treatment of DBT-2. Controlling the progressive decline of cell function is critical because it can lead to glycemic control loss. Conventional medicines and insulin can help, but they can't fix the underlying metabolic and glucoregulatory issues. The threat of diabetes is growing by the day, and vigorous and targeted combinational therapy, notably incretin-based therapy and peptide analogues, is urgently needed. This may help to restore and maintain cell function while also slowing the progression of DBT-2 (Campbell et al., 2009).

In today's world, a new drug's usefulness and success will be determined by its capacity to treat/relieve one or more metabolic abnormalities, such as increased insulin production or improved glucose absorption and utilisation by peripheral tissues, notably skeletal muscle. Aside from new generations of therapies, several other classes have been described as potential ways for treating diabetes, either alone or in combination. The future of leptin therapy is one of the newest concepts in diabetes management. It's a hormone produced by adipocytes that affects the central nervous system's neurons. This hormone has a number of functions, including preventing excessive weight gain by reducing food intake and increasing energy expenditure (Elmquist et al., 1999). Through the activation of leptin receptors (LEPRs), leptins also regulate glucose homeostasis I(Coppari et al., 2005, Huo et al., 2009, Morton et al., 2005). It has been demonstrated that the central nervous system regulates leptin's sugar-lowering effect; it was previously thought that leptin's antidiabetic action could have been affected by DBT-1-related neurons in the brain. In mice with insulin-deficient DBT-1, leptin treatment improves their condition through CNS-dependent pathways (German et al., 2009, Fujikawa et al., 2010).

Designing and using mucoadhesive microcapsules of various medications, such as glipizide, to enable controlled drug release and successful targeting is another area of drug development. Mucoadhesion is a novel strategy in drug delivery design because it causes the drug to release slowly at the action or absorption site, strengthening the drug's interaction with the underlying tissue forms and therefore increasing drug bioavailability (Chowdary et al., 2004, Odegaard et al., 2007). There is no end to the drug delivery methods that have been tried as a possible diabetes cure. (http://www.ondrugdelivery.com/, 2006) The transdermal insulin administration strategy (which was created as a result of painful and difficult insulin therapy) maintains stable insulin levels without the deposits of insulin in the skin that are common with subcutaneous insulin injections. Odegaard and colleagues discovered that activated macrophages have a favourable function in the regulation of nutritional homeostasis, implying that polarising macrophages to the alternate state could be a valuable option in the treatment of DBT-2. Clinical advances have been achieved in the prevention, development, and treatment of the condition, but no therapeutic strategy has yet proven to be totally effective. The search for an effective drug is not far off, thanks to emerging technologies that are transforming treatment options. Diabetes research has been changed thanks to considerable study that led to the discovery of disease-causing pathway genes and the sequencing of entire genomes.

The introduction of tools like as polymerase chain reaction (PCR), DNA microarray, and gene knockouts with silence has opened up a new arena in the identification of faulty genes/mutations in an organism's genome. Diabetes is becoming more common over the world, putting a costly strain on each country's economy. All bioactive treatments have been demonstrated to be beneficial in the treatment of diabetic complications and in lowering blood glucose levels in diabetics with DBT-1. Natural oral treatment also significantly lowered glucose levels and insulin requirements in DBT-1 patients, but more clinical research is needed to determine the exact mechanism (Bhati et al., 2014, Charde et al., 2011, Mourya et al., 2017, Bajaj et al., 2012, Pandey et al., 2016, Shahnawaz et al., 2019, Tiwari et al., 2020).

CONCLUSION

We summarized significant of medicinal plants, treatment therapies, and bioactive ampounds for the treatment of diabetes mellitus in this review. These plants exhibit hypoglycaemic properties, according to the study. Anti-diabetic activity has been discovered in a number of novel bioactive compounds derived from herbal plants. Several other bioactive compounds derived from medicinal plants, on the other hand, have yet to be fully described. In addition, research into the mechanism of action of herbal plants with anti-diabetic properties is required. Simultaneously, this review study has revealed various mechanisms of action and active components in plants, greatly improving our understanding of the rationale underlying popular use of some plants for the prevention and treatment of diabetic complications, allowing us to develop effective medicines for the prevention and treatment of diabetic complications. It's also important to figure out what these herbal plants' adverse effects are. To recognise their medicinal usage and possible anti-diabetic effects, we concentrated on herbal plants from a variety of families. An effort has been made in this review to examine antidiabetic medicinal plants, which may be of great benefit to health practitioners, researchers, and academics working in the field of pharmacology and therapeutics.

Declaration: *We also declare that all ethical guidelines have been followed during this work and there is no conflict of interest among authors.*

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