

HERBAL TREATMENT OF MICROVASCULAR AND MACROVASCULAR COMPLICATIONS OF DIABETES: A REVIEW

Garima Dhingra^{1*}, Sonia Tanwar¹, Kartik Tanwar², Saloni Goyal¹ and Varunesh Chaturvedi¹

¹Research Scholar, School of Pharmaceutical Sciences, Jaipur National University, Jaipur-302017.

²Department of Physiotherapy, PGIMS, Rohtak-124001.

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*Corresponding Author

Garima Dhingra

Research Scholar, School of
Pharmaceutical Sciences,
Jaipur National University,
Jaipur-302017.

ABSTRACT

Herbal drugs, plant medicine, and agricultural medicine are all synonyms for the use of plants as medicine. In comparison to conventional medicine, the medicative use of herbal drugs in the treatment of various diseases such as hyperglycemia has an ancient legacy. Hyperglycemia is one of the major global health interests. Hyperglycemia, also known as diabetes mellitus, is a prevalent matter of public health that is still difficult to manage. Uncontrolled diabetes or sustained hyperglycemia has the potential to cause severe health problems such as renal failure, loss of sight, heart disease, and lower-limb deformities, all of which make a significant contribution to diabetes incidence and death. Herbal drugs are one of the treatment

options to manage and prevent diabetes along with its associated complications. Nevertheless, the choice of herbs may be influenced by a number of aspects, including the level of diabetes development, the types of comorbid conditions that the patients have, accessibility, price, and the clinical efficacy of the herbs. This study concentrates on the naturally - derived therapies that play a role in the management of this distressing disorder – diabetes, together with their biological causes for blood glucose reducing properties and herbal supplements that have already been introduced into the market for therapeutic intervention of diabetes.

KEYWORDS: Diabetes mellitus, Herbal medicines, Microvascular, Macrovascular, Cardiovascular diseases, Retinopathy, Neuropathy.

INTRODUCTION

Diabetes mellitus, or hyperglycemia, is a biochemical condition that results in excessive blood sugar levels. Diabetes occurs when the body either does not produce enough insulin or does not use the insulin that it does produce adequately.^[1] As per the 7th edition of the Diabetes Atlas, the worldwide incidence of diabetes is approximated to be 415 million (8.8 percent), with an increase to 642 million within next 25 years. Furthermore, estimated 193 million diabetics are not diagnosed worldwide, possibly leading them to the progression of various long-term ailments of uncontrolled high blood glucose levels.^[2]

Types of Diabetes

Diabetes is classified into several types. Diabetes type 1, which is an autoimmune disorder. In this, the immune system targets and damages cells of the pancreas, in which insulin forms. It is unknown what is causing this attack. This kind affects around 10% of diabetics. Diabetes type 2, develops when the body gets resistant to insulin, causing sugar to accumulate in the blood. Prediabetes is defined as having blood sugar levels that are higher than usual but not high enough to warrant a risk of type 2 diabetes. Gestational diabetes is defined as elevated blood sugar levels throughout pregnancy. This kind of diabetes is caused by insulin-blocking substances generated by the placenta.^[3] Diabetes symptoms include excessive hunger, dehydration, loss of weight, increased urination, impaired vision, excessive fatigue, and lesions that do not heal. Men with diabetes may have reduced desire for sex, erectile dysfunction (ED), and inadequate physical strength, in addition to the normal symptoms of diabetes. Diabetes can cause symptoms such as urinary infections, yeast infections, and skin irritation in women.^[4]

Each form of diabetes has its own set of reasons. Type 2 diabetes is caused by a mix of hereditary and environmental factors. Becoming overweight or obese also raises the risk. Carrying additional weight, particularly around the abdomen, makes the cells more sensitive to the actions of insulin on blood sugar. This disease runs in families. Members of the family inherit genes that make them more prone to type 2 diabetes and obesity.^[5] Certain variables enhance your chances of developing diabetes. Obesity, being 45 or older, having a parent or sibling with the illness, not being fit and active, having gestational diabetes, prediabetes, hypertension, high blood cholesterol, or triglyceride levels, all raise a person's risk for type 2 diabetes.^[6] High blood sugar levels harm organs and tissues all throughout the body. The higher the blood sugar level and the longer a person has it, the greater the danger of

complications. Diabetes complications include cardiovascular disease, cardiac arrest, and stroke, neurotoxicity, nephropathy, retinopathy and eyesight loss, loss of hearing, foot injury such as abscesses and unhealed ulcers, skin problems such as microbial infections, stress, and memory loss.^[7]

Management of Diabetes

Some patients with type 2 diabetes can benefit from a healthy diet and regular exercise. If lifestyle adjustments are insufficient to lower blood sugar levels, the person may need to take medicine. The medications work in a wide variety of ways to reduce blood sugar levels. It is possible that the patient will need to consume more than one of the medications. Insulin is also used by certain persons with type 2 diabetes.^[8] Diabetes management begins with a healthy diet. In certain circumstances, simply modifying one's diet may be sufficient to control the sickness. Eating the appropriate foods can assist regulate blood sugar and help with weight loss. Carbohydrate counting is an essential aspect of type 2 diabetic diet. A nutritionist can assist you in determining how many grammes of carbohydrates to consume at each meal. Eat modest meals throughout the day to keep diabetes levels under control. Healthy foods such as fruits, vegetables, whole grains, lean protein such as poultry and fish, and healthy fats such as olive oil and nuts should be prioritised.^[9]

COMPLICATIONS OF DIABETES

The complications of diabetes can be acute and chronic. Acute complications include hypoglycaemia, diabetic ketoacidosis and hyperosmolar hyperglycaemic state. Chronic complications are further of two types, microvascular and macrovascular. Microvascular complications include diabetic nephropathy, diabetic retinopathy and diabetic neuropathy. Macrovascular complications include peripheral artery disease, arteriosclerosis and other heart diseases.^[10]

Hypoglycaemia is caused by insulin therapy, oral hypoglycaemic agents, skipping a meal, inconsistent carbohydrate intake, over exercising and alcohol consumption. The signs and symptoms include adrenergic symptoms, caused by activation of sympathetic nervous system and neuroglycopenic symptoms, caused by depression by central nervous system activity as the brain receives an insufficient supply of glucose.^[11]

Adrenergic symptoms result from rapid drop in glucose and occur first, including pale, sweaty, tachycardia/palpitations, nervousness, irritability, cold feeling, weak, trembling and

hunger. The particular signs and symptoms vary depending on the blood glucose levels, how fast the glucose level dropped and the duration of hypoglycaemia.^[12] When the hypoglycaemia is slow developing, as with long-acting insulin or with oral hypoglycaemic agents, the central nervous system signs and symptoms predominate. Those signs include headache, mental confusion, numbness around the mouth, incoherent speech, double vision, fatigue, emotional liability, convulsions and coma. If a rapid drop in blood sugar occurs and is allowed to persist, both the sympathetic and central nervous system signs usually occur.^[13]

The diabetic patient should be educated about recognizing signs and symptoms of hypoglycaemia and how to treat it. As long as a patient is conscious, they should self-treat with 15g of quick-acting carbohydrate, such as 40oz of juice (no added sugar), 3-4 glucose tablets, or 3 hard candies. Recheck the fingerstick blood glucose in 15 minutes and if it remains below 60, the patients should self-treat again. In an unconscious patient, never try to give oral glucose. In the hospital setting, one ampule of 50% dextrose is given IV push.^[14] In an outpatient setting, a friend or family member can inject 1 mg of glucagon subcutaneously, which causes the liver to release its glycogen store. The patient will usually regain consciousness within 10-20 minutes and should then eat a snack of 45g of carbohydrates to aid in replacing glycogen stores. Patients may often be nauseated after receiving glucagon and may vomit. When hypoglycaemia is severe, seizures may also occur.^[15]

Diabetic ketoacidosis is another serious acute complication when excess blood acids called ketones, build up in the body. Ketones are formed when the body burns fat for fuel instead of glucose. This can occur when there is not enough insulin in the body to process sugars. Diabetic ketoacidosis is triggered by illness or not taking insulin. The progressive hyperglycaemia causes glucose to spill out into the urine, resulting in water and electrolyte losses, causing dehydration and increase in thirst.^[16] The lack of insulin and corresponding evaluation of glucagon leads to increased release of glucose by the liver as well as ketone bodies, which are acidic and must be cleared from the circulation. Diabetic ketoacidosis can occur in patients with type 1 diabetes or type 2 diabetes but it is rare with type 2. Risk for diabetic ketoacidosis is increased with type 1 diabetes, under age 19, stress, physical or emotional trauma, high fever, heart attack, stroke, smoking or drugs/alcohol.^[17] Signs and symptoms of diabetic ketoacidosis include high blood sugar levels, high levels of ketones in urine, fruity smelling breath, flushed face, nausea and vomiting, abdominal pain, rapid deep gasping breaths, frequent urination, extreme thirst, dry mouth and skin, weakness, confusion

and loss of unconsciousness. If left untreated, diabetic ketoacidosis can lead to coma and death. Treatment involves rehydration with IV fluids, insulin therapy and electrolyte replacement.^[18]

Hyperglycaemic Hyperosmolar Non-Ketotic Syndrome (HNNS) has some similarities to diabetic ketoacidosis, but is an acute complication of type 2 diabetes. The differences include profound dehydration, with fluid deficit as high as 8-9 litres. Blood sugar levels are higher, with serum glucose levels in the range of 600-2000. Ketosis is absent because patients with type 2 diabetes have insulin secretion to prevent ketosis.^[19] The kidneys try to get rid of the extra blood sugar by putting more glucose into the urine, which increases urination and loss of body fluids, causing dehydration. Dehydration makes the blood thicker and the blood sugar level is too high for the kidneys to be able to fix. This also causes an imbalance of minerals in the blood, especially sodium and potassium. This imbalance of fluids, glucose and minerals in the body can lead to severe problems, such as brain swelling, abnormal heart rhythms, seizures, coma or organ failure.^[20] Without rapid treatment, HNNSs can cause death. Primary treatment involves IV rehydration, which resolves the hyperglycaemia, so IV insulin is usually not needed.^[21]

Chronic complications are of two types, microvascular and macrovascular complications. These complications are a result of the length and degree of hyperglycaemia.^[22]

MICROVASCULAR COMPLICATIONS

Diabetes microvascular complications are long-term health issues that influence small blood vessels. Healthcare professionals have long reported that patients with comparable timespan and intensity of hyperglycemia differ significantly in their sensitivity to microvascular complications. Microvascular complications are prevalent in type 2 diabetes (T2D) patients and make a significant contribution to the rates of morbidity and mortality with this condition. As a result, preventing or halting the transition of these health problems is a major goal of treatment in T2D patients.^[23] Despite the benefits of strenuous metabolic control, these health problems are still common. Lay people have been most concerned about microvascular complications, which is understandable given that diabetes is the leading cause of visual impairment and kidney failure in the non-geriatric community.^[24]

Retinopathy was found in 85 percent of aged people with diabetes, but non-growing retinopathy was far more common than growing ones. Ageing process also

contributes to the rise of renal insufficiency, as well as the age-related onset of diabetes-related renal dysfunction.^[25] Diabetes impairs white blood cell function, which inhibits recovery, as well as vasculature impairment, which prevents healing of wounds. Wounds heal more slowly as a result of the immune compromise caused by diabetes, specifically obstruction with white blood cell chemotactic and leukocyte killing potential.^[26] The most prevalent microvascular complication of diabetes is diabetic retinopathy. Every year, it causes 10,000 new cases of loss of vision in the United States alone. The probability of having diabetic retinopathy or other microvascular complications of diabetes is proportional to both the duration and severity of hyperglycemia. In type 2 diabetes patients, retinopathy can develop as early as 7 years even before onset of diabetes.^[27]

There are many presented pathophysiological processes through which hyperglycemia can cause retinopathy. The enzyme aldose reductase may play a role in the progression of diabetes complications. The first enzyme in the cytoplasmic polyol pathway is aldose reductase. The transformation of glucose into sorbitol is part of this pathway.^[28] High blood glucose levels rise sugar molecule circulation through the polyol pathway, resulting in sorbitol deposition in cells. The progression of diabetic microvascular complications, such as diabetic retinopathy, has been linked to osmotic stress caused by sorbitol deposition. Oxidative stress may also contribute in hyperglycemia-induced cellular injury. High glucose levels can promote the formation of free radicals and reactive oxygen species.^[29] Treatment with antioxidants, such as vitamin E, has been shown in animal studies to reduce some vascular dysfunction hyperglycemia, but intervention with antioxidant compounds has not yet been shown to change the growth of retinopathy and perhaps other microvascular diabetes mellitus.^[30]

Herbal Treatment

Parsley, which contains carotenoids such as lutein, beta carotene, and zeaxanthin, has strong antioxidant properties and can enhance eyesight. Fennel is high in nutrients that are proven to enhance vision. It is also identified as 'the herb of sight,' and it can improve eyesight by retarding the progression of cataracts.^[31] To reap the most benefits, crush fennel seeds with almonds and sugar and consume the powder daily before going to bed. Wild Asparagus is high in antioxidants and can safeguard eyes by preventing free radicals from destroying the retina. Wild asparagus is also high in the amino acid glutathione, which lowers your chances of having night blindness and cataracts.^[32]

Diabetes nephropathy is also a major cause of kidney failure. Proteinuria greater than 500 mg in 24 hours in the presence of diabetes is defined, but this is accompanied by reduced levels of proteinuria, known as "microalbuminuria." Albumin efflux of 30-299 mg/24 hours is considered as microalbuminuria. Diabetics with microalbuminuria usually progress to proteinuria and observable diabetic nephropathy if they do not receive treatment.^[33] Both type 1 and type 2 diabetes experience this transition. Metabolic abnormalities to the kidney involve greater glomerular basement membrane width, the formation of microaneurysms, the formation of mesangial nodules, and other changes. The fundamental cause of injury may include some or all of the mechanisms associated in diabetic retinopathy. A 24-hour urine sample collection or a spot urine microalbumin measurement can be used to screen for diabetic nephropathy or microalbuminuria.^[34] The microalbumin-to-creatinine ratio can be used to compensate for urine concentration or dilution, and spot dimensions are more effective for patients than 24-hour urine sample collections. It is significant to mention that situations such as urinary infections, workout, and blood in the urine can all cause mistakenly raised urinary protein content.^[35] The first defense mechanism against diabetic nephropathy, as with other diabetes complications, is way to reduce the risk. There are significant relationships between blood sugar control and the probability of having diabetic nephropathy, just as there are with other microvascular diabetes complications.^[36] To avoid or regulate diabetic nephropathy, people should be monitored to the minimum possible secured glucose level. Patients with diabetic nephropathy benefit from antihypertensive medication in addition to intensive treatment of high blood glucose levels. Renin-angiotensin system inhibition has numerous advantages in diabetic nephropathy patients rather than simply lowering blood pressure.^[37] Numerous research findings have shown that ACE inhibitors and angiotensin receptor blockers (ARBs) have reno-protective effects that seem to be present independently of their blood pressure-lowering effects, probably due to decreased intraglomerular pressure. Both ACE inhibitors and ARBs have been shown to reduce the risk of steady progress to macroalbuminuria by up to 60% in patients with microalbuminuria. Even in patients who do not have hypertension, these medicines are highly suggested as the first-line therapeutic intervention for microalbuminuria.^[38]

Herbal Treatment

In clinical practise, the main approaches for alleviating albuminuria and treating diabetic patients with diabetic nephropathy are to lower blood pressure, regulate blood sugar, and regulation of dyslipidaemia. Many natural antioxidants, herbs, seeds, and plant extracts, such

as curcumin, catechins, pterostilbene, cinnamaldehyde, allicin, and others, have been tested in animal models of diabetic nephropathy.^[39]

Diabetic neuropathy is defined as "the clinical features of peripheral nerve abnormalities in diabetics after all other causes have been ruled out." Like other microvascular complications, the probability of having diabetic neuropathy is approximately equal to both the duration and intensity of hyperglycemia, and some people may be predisposed to develop such complications due to genetics.^[40] The exact mechanism of hyperglycemia-induced peripheral nerve injury is unknown, but it is closely attributable to processes such as polyol build-up, AGE damage, and oxidative stress. Diabetes-related peripheral neuropathy can occur in several ways, including tactile, focal/multifocal, and autonomic neuropathy. More than 80% of deformities occur as a result of foot ulcers or injury, which could be caused by diabetic neuropathy.^[41] The most prevalent form of neuropathy in diabetes is chronic sensorimotor distal symmetric polyneuropathy. Patients tend to experience burning, twitching, and "electrical" pain, but they may also experience loss of sensation. Pain may be worse at bedtime in patients who suffer from it. Patients with loss of sensation can express a pain free foot ulceration, so it is critical to understand that the absence of signs does not rule out the occurrence of neuropathy.^[42] A medical assessment demonstrates a loss of sensory sensitivity to delicate touch, vibration, and heat. Deformities in more than one peripheral sensation test are more than 87 percent efficient in identifying neuropathy. Patients usually have a damage of ankle reflex as well. Patients who have managed to lose 10-g monofilament perception are at a significantly increased risk of developing foot ulcers.^[43] Diabetes-related autonomic neuropathy leads to huge morbidity and even risk of death in diabetic patients. Neurological impairment can appear as digestive problems, bowel problems, diarrhoea, anhidrosis, bladder disturbance, sexual dysfunction, muscle rigidity, resting tachycardia, silent infarction, and even cardiogenic shock in most organ systems. Cardiovascular autonomic abnormality is linked to a higher risk of silent myocardial injury and death.^[44] There is no curative therapy for diabetic neuropathy, but several medications are available to cure its clinical signs. The foremost aim of treatment is to stabilize complications from worsening by improving blood sugar control. Some researchers have indicated that controlling high blood sugar and avoiding glycaemic excursions may provide approaches of peripheral neuropathy. Amitriptyline, citalopram, gabapentin, pregablin, and oxycodone have often used to cure pain, but only duloxetine and pregablin have actual evidence for the intervention of painful peripheral diabetic neuropathy.^[45]

Herbal Treatment

Attempting to deal with diabetic neuropathy is a distressing integration that can feel like inhumane treatment at times. The immobility and physical discomfort in feet, lower legs, palms, and upper limbs is incapacitating. Furthermore, neuropathy can cause digestive problems as well as irreversible nerve damage. Managing diabetes requires a healthy diet, and once it is under control, the neuropathy will slow down.^[46] It is advised to control the amount of starch and sugar you consume as they will cause blood glucose levels to rise significantly. Minimize the intake of processed food products and make sure to drink plenty of water daily. It also includes lean proteins, fiber-rich foods, and essential fats in the diet.^[47] Anxiety can cause inflammation throughout the body, exacerbating nerve damage. This may have even related moments of extreme stress to the times of increased nerve damage. If this is the case, work on relaxing and dealing with stress in a constructive way. Relax by meditating, going for a walk, or focusing on a habit.^[48] Receiving a spa treatment or attempting acupuncture may also reduce stress, anxiety and neuropathic pain. Workout benefits the body in a variety of ways, which include assisting in the maintenance of healthy heart rate and blood pressure.^[49] According to research, exercising helps neuropathy patients experience less pain. Workout also aids in the regulation of blood glucose levels.^[50] There are a few organic oils and essential minerals that can take on a regular basis to decrease the level of pain from neuropathy. Cinnamon can assist in controlling blood glucose levels. By adding a couple teaspoons of cinnamon to the food or taking cinnamon probiotics. Some other alternatives for pain relief are to use lavender, peppermint, or frankincense essential oils.^[51] Another anti-inflammatory that could benefit with the burning and loss of sensation is primrose oil.^[52]

MACROVASCULAR COMPLICATIONS

Diabetes-related macrovascular complications are primarily conditions of the coronary arteries, peripheral arteries, and cerebrovascular structure. Atherosclerotic marker in the vascular system willing to supply blood to the heart, central nervous system, extremities, and other body parts is correlated with various macrovascular disease.^[53] Late-stage macrovascular disease causes complete blockage of these vessels, increasing the risk of myocardial infarction (MI), cerebrovascular disease, nerve entrapment, and necrosis. Cardiovascular disease (CVD) is the leading cause of illness and death in diabetic patients.^[54]

Diabetes patients are at an increased risk of developing heart disease, peripheral artery disease, and vascular disease due to macrovascular complications. Hyperglycemia, alone or in combined effect with hypertension, is thought to be responsible for 37 to 42 percent of all ischemic strokes. The incidence of heart disease or stroke in diabetic patients is estimated 34% in both men and women. In diabetic patients aged 30 and up, the incidence of peripheral arterial disease is 26%.^[55]

Diabetes' macrovascular complications are caused by high blood sugar, large amounts of free fatty acid, and glucose intolerance. These increase oxidative stress, activate protein kinases, and activate the binding site for glycation end products, all of which respond on the endothelium.^[56] First, a reduction in nitric oxide, a significantly raise in endothelin, and a rise in angiotensin II cause vascular constriction, which leads to high blood pressure and the progression of vascular smooth muscle cells.^[57] Second, reduced nitric oxide, enabled nuclear factor-KB, enhanced angiotensin II, and stimulation of activated protein-1 all contribute to inflammation, which leads to the activation of cytokines and chemokines as well as the interpretation of cellular adhesion molecules.^[58] Third, thrombosis, hypercoagulation, platelet activation, and reduced fibrinolysis are characterized by reduced nitric oxide, increased tissue factor, enhanced plasminogen activator inhibitor-1, and reduced prostacyclin. These pathways eventually lead to atherosclerosis, which is the root cause of the disease.^[59]

Patients with diabetes-related CVD may show with angina pectoris, myocardial infarction, or irregular heartbeats; even so, several patients have unnoticed clinical signs. Patients suffering from cerebral vascular disease may experience the early symptoms of a neurodevelopmental deficit such as facial wobble, hemiplegia, or lack of strength of limbs.^[60] Symptoms such as drowsiness, difficulty speaking, locomotory challenges, and vision disturbances can also occur. Exertional muscle pain, which can proceed to pain at rest, and ischemic ulcers are symptoms of peripheral vascular disease. Showing no symptoms is the most likely scenario.^[61]

Numerous advanced medical studies can be used to check a cardiovascular diagnosis. A 12-lead electrocardiogram at rest is not sufficient to detect ailment in patients with persistent angina. Cardiac anxiety testing can be performed using electrocardiographic monitoring while exercising, dobutamine, dipyridamole, or adenosine.^[62] Echocardiography can improve the test's responsiveness. Nuclear stress monitoring with thallium 201 or technetium 99m in conjunction with dipyridamole or adenosine is another option. Comparative hypoperfusion in

maximum stress images show substantial coronary artery disease.^[63] Coronary arteriography can indicate the diagnosis of cardiovascular disease. A stroke is diagnosed when a patient develops clinical signs of focal neurologic deficit, which can be stated by a computed tomography scan or imaging tests.^[64]

CT angiography is being used to determine the position of a vascular occlusion and determine whether or not brain tissue can be saved.^[65] The ankle brachial index is used to determine the presence of peripheral arterial disease. This is the ratio of the systolic ankle strain assessed by Doppler to the systolic brachial force. In order to detect peripheral arterial disease, an ankle brachial index less than 0.9 has a response of 95% and a specificity of 100%. An ABI higher than 1.4 indicates that the arteries are calcified. It has been linked to a higher risk of foot ulcers and cardiovascular disease.^[66] Other tests, such as duplex ultrasonography, MR angiography, and CT angiography, could be used to identify particular spots of surgical treatment if revascularization is being regarded.^[67]

The American Diabetes Association's guiding principle is that diabetes is a terrible condition with fatal consequences due to microvascular and macrovascular complications. Careful screening for these complications enables doctors to minimize the risk of their onset and development.^[68] Combative glycaemic control therapies, and also lipid and blood pressure monitoring, appear to have a positive impact on many diabetes - related complications.^[69] Aspirin treatment has been considered to lower the risk of Cardiovascular events in patients. These assessment and treatment approaches are backed up by comprehensive observation - based and treatment trial data and, as a result, are supported by the different organizations that have published disorder management strategy.^[70]

Diabetes and its comorbidities have been linked to long-term progressive destruction of multiple organ systems. Diabetes causes alterations in the microvasculature, resulting in extracellular matrix protein production and capillary basement membrane hypertrophy, both of which are pathogenomic characteristics of diabetic microangiopathy.^[71] These alterations, combined with advanced glycation end products, oxidative stress, sub-standard infection, and vasa vasorum neovascularization, can result in macrovascular complications. Diabetes mellitus is the primary cause of microvasculopathy, but it also believed to play a part in the growth of macrovasculopathy.^[72] Micro and macro vascular complications are thought to collide, but the two situations appear to be strongly linked, with micro vascular ailments facilitating atherosclerosis via procedures such as hypoxic conditions and alterations in vasa

vasorum. It is therefore critical to determine whether microvascular complications come before macrovascular complications or if they progress in unison as a dynamic process.^[73]

Herbal Treatment

Diabetes is analysed in traditional medical systems based on its obvious side effects. Traditional treatment additionally depicts various side effects, for example, severe migraine, fatigue, chest pain and suffering, infrequent heartbeat, and others for the identification of cardiac illnesses. According to a recent study, natural plant assets account for 25% of prescribed medications and 75% of novel medicines used to treat harmful diseases.^[74] *Nigella Sativa* has been used in traditional medicine, and several studies have been conducted in recent years to investigate its effects on a variety of therapeutic issues, for example, diabetes mellitus, dyslipidemia, high blood pressure, and obesity.^[75] *Nigella sativa* oil at a dose of 2.5mg/kg reduces the N-nitro-L-arginine methyl ester (L-NAME)-induced increase in blood pressure and was associated with a reduction in cardiac redox status, angiotensin-changing over catalyst movement, and an increase in heme oxygenase (HO-1) action.^[76]

Broccoli, Brussels sprouts, cabbage, cauliflower, radish, rutabaga, turnip, and even baby spinach is included in Cruciferous vegetables. Because cruciferous vegetables comprise isothiocyanates, which can produce the redox-controlled cardioprotective protein thioredoxin, it was thought that eating broccoli could be beneficial to the heart.^[77] Sulforaphane is by far the most widely distributed and well-studied isothiocyanate. According to research, sulforaphane helps with artery divider irritation, controls obesity, lowers hypertension, and other situations that are a part of or lead to cardiovascular disease.^[78] Temperature ready onion concentrate contains arginyl-fructose, a significant bioactive Amadori advancement compound, as well as phenolic compounds, which have postprandial blood glucose-lowering and anticarcinogenic agent effects.^[79] When compared to other medicinal herbs, the bark of *Terminalia arjuna* incorporates a highly unusual level of flavonoids, specifically arjunolone, flavones, quercetin, kempferol, and pelargonidin. It is widely used to treat cardiovascular diseases, such as heart disease and associated chest pain, high blood pressure, and high cholesterol. Various clinical studies have also revealed its beneficial effects in patients with long-term stable angina, endothelial damage, heart failure, and even myocardial mitral leaking.^[80]

CONCLUSION

Plant utilisation is one of the traditional practices that has been tried to impose on modern society in order to determine the methodology of their fundamental therapeutic effects, as well as the related advantages and disadvantages. Thus, the use of herbal remedies for diabetes management, wellness, and therapeutic interventions is still prevalent in modern society. Production of commercial drugs are mainly obtained from plants and constitute the majority of modern medicine. As a result, several herbs have been demonstrated to have anti-diabetic function by controlling insulin release, glucose tolerance to cells, and other procedures in terms of improving patients' blood sugar control. In addition to blood glucose control, several of the herbs demonstrated efficacy in the prevention of cardiovascular disorders by lowering triglyceride, high cholesterol, and body mass index. Due to a perception of the land and accessibility, herbal remedies have always been favoured medications available by patients or as an adjunctive to traditional therapeutic option for diabetes. As a result, experimental studies have approached the hospital room of the patients through medical studies and commercially available formulations. Even so, the rapid development of the ethnopharmaceutical domain in the management of diabetes necessitates the urgent development of valid and reliable screening procedures in order to assess the number and yield of active pharmaceutical ingredients present in the finished products, which will then need to be evaluated on human volunteers through well-designed clinical trials, proved and accredited by the country's affiliated regulatory bodies in terms of building purchaser trust and satisfaction in efficacy of the product and services.

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CONFLICT OF INTEREST

None.

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