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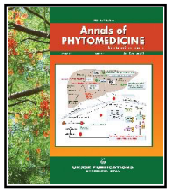

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Type 2 Diabetes mellitus: Current prevalence and future forecast

Putta Swetha* and Malarkodi Velraj**◆

**Department of Pharmacology, School of Pharmaceutical sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS). Pallavaram, Chennai-600117, Tamilnadu, India*

***Department of Pharmacognosy, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS), Pallavaram, Chennai-600117, Tamilnadu, India*

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Abstract

It has been determined that diabetes mellitus is one of the four most significant non-communicable illnesses, and as such, it requires immediate attention from all of the key stakeholders throughout the world in an effort to reduce its prevalence and the difficulties that are connected with it. In light of the consequences of hyperglycemia, as well as hyperglycemic-induced oxidative stress and inflammation, it is regarded to be one of the top 10 major causes of mortality throughout the world, and it is responsible for the deaths of around 1.6 million people each and every year. Additionally, it is regarded as the third most significant risk factor for the premature death of people throughout the world. There is a significant connection between hyperglycemia, hyperglycemic-induced oxidative stress, inflammation, and the onset and progression of type 2 diabetes mellitus. Reports from a variety of sources have demonstrated that persistent low-grade inflammation is connected to an increased chance of developing type 2 diabetes, and that sub-clinical inflammation is a contributor to insulin resistance and is linked to the hallmarks of metabolic syndrome, which include hyperglycemia. Both of these findings are consistent with one another. The fundamental impetus behind the objective of this review was the relationship that exists between diabetes, oxidative stress, and inflammation. By conducting large number of research work, numerous traditional medicines have been found for diabetes. Extracts isolated from different natural resources especially plants, have always been a rich arsenal for controlling and treating diabetes problem and complication arising due to it. Therefore, the reader is able to have a better understanding of the significance of the many different herbal and polyherbal formulations that have historically been used to treat diabetes mellitus as a result of reviewing this article.

1. Introduction

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia resulting from defects in insulin secretion, insulin action, or both. Metabolic abnormalities in carbohydrates, lipids, and proteins result from the importance of insulin as an anabolic hormone. Skeletal muscles, adipose tissue, and to a lesser extent, liver, at the level of insulin receptors, signal transduction system, and/or effector enzymes or genes are responsible for these metabolic abnormalities. The severity of symptoms is due to the type and duration of diabetes. Some of the diabetes patients are asymptomatic especially those with type 2 diabetes during the early years of the disease; others with marked hyperglycemia and especially in children with absolute insulin deficiency may suffer from polyuria, polydipsia, polyphagia, weight loss, and blurred vision. Uncontrolled diabetes may lead to stupor, coma and if not treated death, due to ketoacidosis or rare from nonketotic hyper osmolar syndrome (Mohamed, 2014; Moss and Mathews, 2013).

Corresponding author: Dr. Malarkodi Velraj
Professor Department of Pharmacognosy, School of Pharmaceutical Sciences, Vels Institute of Science, Technology and Advanced Studies (VISTAS). Pallavaram, Chennai-600117, Tamilnadu, India
E-mail: malarkodiv.sps@velsuniv.ac.in
Tel.: +91-9884242196

Diabetes mellitus (DM) is a major public health issue affecting more than 400 million people worldwide. This metabolic disorder progressively leads to chronic microvascular, macrovascular and neuropathic life threatening complications. DM is caused either by deficiency of insulin secretion, damage of pancreatic β cell or insulin resistance related to down regulation of insulin receptors. Inclination to sedentary lifestyle may be the major reason for the continual rise in the number of diabetic patients globally which is expected to strike 366 million in 2030 in the elderly population (>65 years) (Bayramova, 2016). The various complications associated with DM includes nephropathy, neuropathy, cardiovascular and renal complications, retinopathy, food related disorders and so on. Type 1 DM and type 2 DM are the 2 types of DM. T1 DM is an autoimmune disorder that affects pancreatic cells which reduces or impairs the production of insulin while T2 DM is a result of impairment of pancreatic beta cells that hinder the individual's ability to use insulin.

2. Etymology of diabetes mellitus

The word diabetes originates from Latin diabetes, which thusly originates from Ancient Greek, which actually signifies "a passer through; a siphon". Ancient Greek doctor Aretaeus of Cappadocia (fl. first century CE) utilized that word, with the planned signifying "exorbitant release of pee", as the name for the disease. "Diabetes" is initially recorded in English, in the structure diabetes, in a medicinal

content composed around 1425. The word mellitus originates from the traditional Latin word mellitus; signifying "mellitus" (*i.e.*, sweetened with honey, nectar sweet). The Latin word originates from mell-, which originates from mel, signifying "honey", and the postfix - îtus, whose importance is the same as that of the English addition "- ite". It was Thomas Willis who in 1675 included "mellitus" to "diabetes" as an assignment for the infection, when he saw the pee of a diabetic had a sweet taste (glycosuria) (Kulathuran Pillai Kumaraswamy *et al*., 2022; Tagliente, 2016).

3. History of diabetes mellitus

Diabetes was one of the primary diseases described, with an Egyptian original copy from c. 1500 BCE saying "excessively extraordinary exhausting of the urine". The initially depicted cases are accepted to be of type 1 diabetes. Indian doctors around the same time distinguished the sickness and characterized it as madhumeha or "nectar pee", noticing the pee would pull in ants. The word "diabetes" or "to go through" was initially utilized as a part of 230 BCE by the Greek Apollonius of Memphis. It was viewed as uncommon amid the season of the Roman realm, with Galen remarking he had just seen two cases amid his career. This is perhaps because of the eating regimen and way of life of the people of old, or because the clinical indications were seen amid the advanced phase of the illness. Galen named the diseases "looseness of the bowels of the pee" (diarrhoea urinosa). The soonest surviving work with a point by point reference to diabetes is that of Aretaeus of Cappadocia (second or mid third century CE). He portrayed the manifestations and the course of the illness, which he ascribed to the dampness and coldness, mirroring the convictions of the "Pneumatic School". He conjectured a connection of diabetes with different maladies and he examined differential conclusion from the snake bite which additionally incites exorbitant thirst. His work stayed obscure in the West until 1552, when the main Latin release was distributed in Venice. Type 1 and type 2 diabetes were recognized as independent conditions interestingly by the Indian doctors Sushruta and Charaka in 400-500 CE with type 1 connected with youth and type 2 with being overweight. The expression "mellitus" or "from nectar" was included by the Briton John Rolle in the late 1700s to isolate the condition from diabetes insipidus, which is additionally connected with regular urination. Effective treatment was not created until the early part of the twentieth century, when Canadians Frederick Banting and Charles Herbert Best separated and sanitized insulin in 1921 and 1922. This was trailed by the improvement of the long-acting insulin NPH in the 1940s.

4. Classification of diabetes

Classification is based on the production of insulin by the pancreas or the cells of the body response properly towards the insulin production. There are three main types of diabetes mellitus:

4.1 Type 1 diabetes mellitus

In this type of diabetes, pancreas does not produce insulin properly or no insulin is produces by pancreas. It is also known as insulin dependent diabetes mellitus (IDDM) or juvenile diabetes or early onset diabetes. The causes for T1 diabetes are unknown. It is less common than type 2, generally only 10% of all diabetes case is type 1. Patients suffering from type 1 diabetes should take insulin injections for rest of their life. They should likewise guarantee appropriate blood-glucose levels *via* doing consistent blood tests and taking after an uncommon eating routine (Shabnam Ain *et al*., 2022).

4.2 Type 2 diabetes mellitus

In type 2 diabetes, the body does not produce enough insulin to address its own particular issues or cell does not respond properly against the insulin. This is known as insulin resistance. Type 2 diabetes is also known as "non-insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes". It happens in 75 to 90% of all instances of diabetes. Type 2 diabetes as a rule grows steadily after some time. Most people with the condition might be ignorant of their ailment particularly at early stages as there might be no particular side effects. Type 2 diabetes is frequently connected with weight (Ignacio, 2016). Corpulence related diabetes is now and then alluded to as development onset diabetes since it is more normal in more seasoned individuals. In numerous early instances of type 2 diabetes, treatment might be conceivable by simply eating a solid eating regimen and checking blood glucose levels routinely. In any case, as type 2 diabetes is a dynamic condition in the long run medicines might be required. There are a few gatherings of oral pills that can be taken to control the glucose. In some serious type 2 diabetes, insulin administration might be vital.

4.3 Gestational diabetes

It is the third type of diabetes. This type affects female during pregnancy. A few women have large amounts of glucose in their blood, and their bodies can not create enough insulin to transport the greater part of the glucose into their cells, bringing about dynamically rising levels of glucose. Pregnant women with gestational diabetes could conceivably have prior type 1 or type 2 diabetes. Much of the time, gestational diabetes creates amid the second trimester of pregnancy (weeks 14-26) and vanishes after the child is conceived (Szybinski, 2016; Zeyad Allahabi and Sanjeev Singh, 2022). Gestational diabetes can build the danger of wellbeing issues creating in an unborn infant. The diagnosis of gestational diabetes is typically established over the course of pregnancy. The dominant part of gestational diabetes patients can control their diabetes with activity and healthy diet. Between 10% to 20% of them should take some type of blood-glucose-controlling solutions. Undiscovered or uncontrolled gestational diabetes can raise the danger of entanglements during labour.

4.4 Other specific type of diabetes mellitus

It is into MODY (maturity onset diabetes of young), LADA (latent autoimmune diabetes in adults) and endocrinopathies. It is also caused by genetic abnormalities in the internal secretion of insulin hormone.1 to 5% of people who have suffered from it develop by mutations. This includes diseases of the pancreas, certain surgeries, genetic defects in beta cells, cancer therapies, medications and infections, *etc*. Some medicines are utilized or mixed with the treatment of HIV /AIDS or organ transplantation.

4.4.1 MODY

MODY is inherited diabetes mellitus by a genetic mutation in an autosomal dominant gene that affects the secretion of insulin secretion or production and it is not an insulin dependent diabetes. Individual diagnosis is generally in childran less than age 25 with genetic factors. HNF1-α (hepatocyte nuclear factor) gene causes about 70% of cases of MODY. It associates with a genetic defect of the β-cells. In this

type occurs hyperglycemia at an early age. They are clinically closer to T2 DM (Parveen and Anjum, 2016; Hines and Kumar, 2016).

4.4.2 LADA

In this, the patients do not produce any insulin and it is clinically similar to T1 DM, LADA occurs because pancreatic cells stop insulin production. LADA is present in young adults in their twenties and can be confused with type 2 diabetes mellitus because of age. T1 DM are different from LADA (Vikash Gupta and Mohan Lal Kori, 2022).

4.4.3 Endocrinopathies

Several hormones play activity on insulin action or inhibit insulin action. Impaired fasting blood glucose presents as an FBG higher than 100 mg/dl, but less than 126 mg/dl. It may include polycystic ovarian syndrome, pancreatic cancer or tumours and other hormonal disruptions in insulin production.

5. Etiology of diabetes mellitus

Sometimes, chemicals and drugs are causes T1 DM. Its cause's autoimmune disorders such as Graves' disease, Hashimoto's thyroiditis and Addison's disease. Which can seriously causes that type of diabetes mellitus. In about 70-80% of cases, beta-cells are destroyed the immune system. In T1 DM, the beta cells fail to produce insulin. T1 DM is commonly caused by the destruction of beta-cells. The cause of this autoimmune response is unknown T1 DM characterized by antiglutamic acid decarboxylase. Due to improper use of insulin, the glucose level decreased in the body, the leading cause of T2 DM. It is also caused by overeating, smoking, alcoholism, dysfunction of the endocrine and nervous system. 33% of American adults have higher kidney disease. African Americans, Latinos, Native Americans, Asian Americans, and Pacific Islanders all have a high risk of kidney disease. In T2 DM, the body fails to utilize insulin. Some traditional groups have a higher inherited incidence of it. The body produces a hormone called Insulin that maintains normal blood sugar levels. During pregnancy, the placenta produces higher pregnancy hormones that can interfere with insulin. The body can make more insulin during pregnancy to keep blood glucose levels normal (Hayashi and Suganuma, 2016). Still, in some women, the body cannot make sufficient insulin during pregnancy and blood sugar levels increases and causes GDM. The main cause of diabetes retinopathy is blindness and it causes 2.6% of global blindness.

6. Pathophysiology of diabetes mellitus

6.1 Physiological mechanisms

6.1.1 The endocrine pancreas

The human pancreas is basically composed of two types of secretory cells that are both involved in nutrient handling: 98% of the cells, the exocrine type, secrete a food processing enzyme and bicarbonate mixture into the duodenum, while the remaining 2%; the endocrine type, have a metabolic function and secrete a mixture of nutrient and generated hormones into the portal vein. This small endocrine part is of vital importance in maintaining glucose homeostasis through the action of the 51-amino acid peptide insulin. Four endocrine cell types can be distinguished: A cells (alpha), B cells (beta), D cells (delta) and PP cells (pancreatic polypeptide). These endocrine cells are distributed throughout the pancreas in areas known as islets.

6.1.2 Diabetes-related islet changes

The islet changes, from a morphological point of view, associated with various types of diabetes can be divided into those with and without severe beta-cell loss. Severe beta-cell loss is found in type 1 diabetes and some uncommon forms of diabetes such as virus-related diabetes and congenital diabetes (Lambadiari, 2016). Islets without severe loss of beta-cells are encountered in type 2 diabetes and in the secondary forms of diabetes.

6.1.3 Insulin

The beta-cells of the pancreatic islets synthesize insulin from a single chain precursor of 110 amino acids termed preproinsulin. After translocation through the membrane of the rough endoplasmic reticulum, the 24-amino-acid N-terminal signal peptide of preproinsulin is rapidly cleaved off to form proinsulin. Here, the molecule folds and the disulfide bonds are formed. On the conversion of human proinsulin to insulin in the golgi-complex, four basic amino acids and the remaining connector or C peptide are removed by proteolysis. This gives rise to the two-peptide chains (A and B) of the insulin molecule, which contains one intra-subunit and two inter-subunit disulfide bonds. The A chain usually is composed of 21 amino acids and the B chain 30. The two chains of insulin form a highly ordered structure with several helical regions in both the A and B chains (Wu, 2016; Abdulrhman, 2016).

Two ions of Zn^{2+} are coordinated in a proinsulin hexamer and this form of insulin presumably is stored in the granules of the pancreatic β cells. It is believed that Zn^{2+} has a functional role in the formation of crystals and that crystallization facilitates the conversion of proinsulin to insulin, as well as the storage of the hormone.

6.1.3.1 Insulin secretion

Insulin is released from pancreatic β-cells at a low basal rate and at a much higher rate in response to a variety of stimuli, especially glucose. Hyperglycaemia results in increased intracellular ATP (adenosine triphosphate) levels, which close the ATP-dependent potassium channels. Decreased outward potassium current through this channel results in depolarization of the β-cell and the opening of voltage-gated calcium channels. The resulting increased intracellular calcium triggers the secretion of the hormone.

6.1.3.2 Insulin degradation

The liver and kidney are the two main organs that remove insulin from circulation, presumably by hydrolysis of the disulfide connection between the A and B chains through the action of glutathione insulin transhydrogenase (insulinase). After this, reductive cleavage further degradation by proteolysis occurs. The liver normally clears the blood of approximately 60% of the insulin released from the pancreas by virtue of its location as the terminal site of the portal vein blood flow, with the kidneys removing 35-40% of the endogenous hormone. However, in insulin-treated diabetics receiving subcutaneous insulin injections, this ratio is reversed, with 60% of exogenous insulin being cleared by the kidney and the liver removing no more than 30-40%. The half-life of circulating insulin is 3-5 min.

6.1.3.3 The insulin receptor

Once insulin has entered the circulation, it is bound by specialized receptors that are found on the membranes of most cells. However, the biological responses promoted by these insulin-receptor

complexes have only been identified in a few target tissues, *e.g.,* liver, muscle and adipose tissue. The receptors bind insulin with high specificity and affinity in the picomolar range. The full insulin receptor consists of two heterodimers, each containing an alpha subunit, which is entirely extra cellular and constitutes the recognition site, and a beta subunit that spans the membrane. The β-subunit contains a tyrosine kinase. When insulin binds to the alpha subunit on the outer surface of the cell, tyrosine kinase activity is stimulated in the beta portion. Although, the β dimeric form is capable of binding insulin, it does so with a much lower affinity than the tetrameric ββ form. Self-phosphorylation of the β portion of the receptor causes both increased aggregation of β heterodimers and stabilization of the activated state of the receptor tyrosine kinase.

In clinical situations associated with elevated levels of circulating insulin, such as obesity or insulinoma, the concentration of insulin receptors is reduced. This down regulation of insulin receptors seems to provide an intrinsic mechanism whereby the target cells limit their response to excessive hormone concentrations.

6.1.3.4 Effects of insulin on its targets

Insulin promotes the storage of fat as well as glucose within specialized target cells and influences cell growth and the metabolic functions of a wide variety of tissues.

6.1.3.5 Action of insulin on glucose transporters (GLUT)

Insulin has an important effect on several transport molecules that facilitate glucose movement across cell membranes. These transporters may play a role in the etiology as well as the manifestation of diabetes. GLUT 4, quantitatively the most important in terms of lowering blood glucose, is inserted into the membranes of muscle and adipose cells from intracellular storage vesicles by insulin. Defects in GLUT 2 mediated transport of glucose into pancreatic β-cells may contribute to the reduced insulin secretion that characterizes type 2 diabetes.

6.1.3.6 Action of insulin on the liver

The first major organ reached by endogenous insulin *via* the portal circulation is the liver, where its function is to increase storage of glucose as glycogen and to reset the liver to the fed state by reversing a number of catabolic mechanisms, such as glycogenolysis, ketogenesis, and gluconeogenesis, which are associated with the post-absorptive state (Wamique and Ali, 2016). These effects are brought about directly through insulin-induced phosphorylation, which activate pyruvate kinase, phosphofructokinase and glucokinase, while reprieving gluconeogenic enzymes, including pyruvate carboxylase, phosphoenolpyruvate carboxykinase, fructose bisphosphatase, and glucose 6-phosphatase. Insulin also exerts indirect effects to decrease hepatic gluconeogenesis and ketogenesis by reducing the fatty acid flux to the liver through its antilipolytic action on adipocytes. In addition, insulin decreases urea production, protein catabolism, cAMP (cyclic adenosine monophosphate) in the liver, promotes triglyceride synthesis and, increases potassium and phosphate uptake by the liver.

6.1.3.7 Effect of insulin on muscle

Insulin promotes protein synthesis by increasing the amino acid transport and by stimulating ribosomal activity. It also promotes glycogen synthesis to replace the glycogen stores expended by muscle activity. This is accomplished by increasing the glucose transport into the muscle cells, inducing glycogen synthase, and inhibiting glycogen phosphorylase (Da Silva, 2016).

6.1.3.8 Effect of insulin on adipose tissue

Insulin acts on reducing circulating free fatty acids and promoting triglyceride storage in adipocytes by three mechanisms:

i. induction of lipoprotein lipase, which actively hydrolyzes triglycerides from circulating lipoproteins; and

ii. glucose transport into cells to generate glycerophosphate as a metabolic product, which permits esterification of fatty acids supplied by lipoprotein hydrolysis;

iii. reduction of intracellular lipolysis of stored triglyceride by a direct inhibition of intracellular lipase.

7. Diagnosis of diabetes mellitus

Diabetes is diagnosed by testing the blood glucose/sugar levels. Blood is tested before meal some food. Mostly, it is performed in the morning time before breakfast. If, a blood sugar level after fasting is above 125 mg/dl, hence diabetes mellitus is diagnosed. Your doctor will examine blood pressure, weight and feet.

i. Obesity: A condition that greatly raises a person's risk for T2 DM.

ii. High BP: A condition often present in people with T2 DM, that together with diabetes, will increase the risk of cardiovascular diseases.

iii. Weak pulses in the feet: A condition that can prevent or reduce foot sore healing and possibly amputation. To decrease the risk of ulceration.

7.1 Tests for diagnosis GDM

7.1.1 O'Sullivan test

This test is used to examine GDM. A fasting patient is given 50 g of glucose. Blood is drawn at every hour. GDM is indicated by plasma levels above 1500 mg/dl

8. Treatment of diabetes mellitus

T1 DM is unavoidable because it is caused by a problem with the immune system. Most diabetes prevention or treatment strategies involve making simple changes to diet and fitness routine. Some causes of T2 DM, such as genes or age, are out of control. Yet, many other diabetes mellitus risk factors are manageable (Parveen and Anjum, 2016). These are not the only ways to prevent diabetes mellitus. Diabetes mellitus is a chronic disease with an unknown cure.

T2 DM can be delayed or prevented by following step:

i. Get at least 20 min/day of aerobic exercises.

ii. If overweight, try to lose 7% as a reliable source.

iii. The diet excludes refined carbohydrates from diet.

iv. Eating many more fruits, vegetables and whole grains daily.

It may be possible to manage by eating healthy foods, exercising, and maintaining healthy body weight.

8.1 Latest drugs in treating diabetes

The burden of diabetes and its difficulties is expanding around the world. To constraint this pandemic, drugs focusing on various regions of the pathogenesis of diabetes and its impediment are required. Inflammation considers a key part in the common history of diabetes amid the movement from pre-diabetes to diabetes, counting diminished beta cell secretory limit and insulin resistance (Ozkum *et al*., 2013; Narayan *et al*., 2012). Insulin resistance is an essential part of the metabolicdisorder and assumes a part in the pathogenesis of different macro vascular entanglements. Drugs focusing on incendiary pathways speak to a new approach in the treatment of diabetes and its complexities.

8.2 Etanercept

Etanercept (934 amino acids, 150 kilo Dalton) is a dimeric combination protein with an extracellular ligand authoritative space of the human tumor necrosis factor receptor (TNFR) connected to the Fc part of human IgG1. It is created by a recombinant DNA strategy in Chinese Hamster ovary cells. Barricade of TNF-α receptor has been appeared to diminish insulin resistance in corpulent rats. A trial of etanercept neglected to enhance insulin affectability in subjects with the metabolic disorder in spite of bringing down CRP. This may have been because of the way that the centralization of TNF-α intracellularly is twice that in the extracellular space, and it is the intracellular TNF-α that is mindful for insulin resistance by means of paracrine impacts which were not obstructed by etanercept (Recent, 2015).

8.3 Anakinra

Anakinra (153 amino acids, 17.3 kilo Dalton) is a non-glycosylated type of the Human IL-1 receptor opponent (IL1Ra) from which it varies just by the expansion of a solitary methionine build up at the amino end. It is created by a recombinant DNA strategy in *E. coli*. IL-1 adds to debilitated insulin emission, diminished cell multiplication, and apoptosis of pancreatic β cells. The IL1Ra is endogenously created, and its focuses are lessened in the pancreatic islets of patients with T2 DM. Anakinra was concentrated on in T2 DM what's more, demonstrated guarantee in expanding beta cell secretory capacity, and diminishing glycemia and markers of systemic inflammation (Kumari *et al*., 2016; Tabatabaeimalazy *et al*., 2015). Authoritative conclusions on the conceivable clinical utility of IL-1Ra in the counteractive action of diabetes are anticipated from the vast continuous canakinumab-antiinflammatory thrombosis outcomes study stage III clinical trial.

The study is being directed in more than 40 nations around the globe and is particularly trying whether hindering the genius provocative cytokine IL-1 β with canakinumab, when contrasted with fake treatment, can lessen rates of intermittent myocardial localized necrosis, stroke, and cardiovascular passing among patients with a background marked by myocardial localized necrosis who stay at high hazard due to a persistent elevation of the inflammatory biomarker hsCRP (p<2 mg/l)

8.4 Sirtuin 1

Sirtuin 1 (Sirt1) is a NAD +-subordinate HDAC class III deacetylase. A portion of the SIRT1 deacetylation substrates (PGc1a, FoXo, p53, and the p65 subunit of NF-κB (10, 41-43 proteins) are focal controllers of cell digestion system, vitality use, irritation and stress reaction pathways in the cell. These might be an extra focus in lessening irritation. Actuation of Sirt1 may have a mitigating part to play in the islets. Sirt1 over-expression forestalls NF-κB interceded cytokine- prompted β cell harm and its demeanor has been appeared to be lessened in pancreatic islets after cytokine exposure.

8.5 Chloroquine

Chloroquine is a feeble base and conveys a positive charge at acidic pH. It is this property of the medication that makes it specifically gather in lysosomes and produce a focus inclination of a high request (Prabhakar and Doble, 2011). This lysosomal atrophic activity is in charge of the hepatic maintenance of insulin. Another activity of the medication is diminished corruption of insulin in the muscle tissue. A review study proposed that the utilization of chloroquine to treat rheumatoid joint inflammation is connected with a lower rate of T2 DM (Reddy *et al*., 2000). Notwithstanding, this study included a particular gathering of patients who required the medication for another sign. Forthcoming investigations of chloroquine are continuous and the outcomes are anticipated.

9. Management of diabetes mellitus

Diabetes mellitus is a disease, for which there is no known cure aside from in particular situations. Management focuses on keeping glucose levels as near ordinary, without bringing on low glucose. This can typically be proficient with a solid eating regimen, exercise, weight reduction, and utilization of suitable meds (insulin on account of type 1 diabetes; oral pharmaceuticals, and additionally potentially insulin, in type 2 diabetes). Finding out about the sickness and effectively taking an interest in the treatment is vital, since entanglements are far less regular and less extreme in individuals who have very much overseen glucose levels. The objective of treatment is an HbA1C level of 6.5%, however might not to be lower than that, and might be set higher. Attention is additionally paid to other wellbeing issues that may quicken the negative impacts of diabetes. These incorporate smoking, lifted cholesterol levels, stoutness, hypertension, and absence of customary exercise. Specialized footwear is broadly used to decrease the danger of ulceration, or re-ulceration, in at-danger diabetic feet. Working intimately with your specialist, you can deal with your diabetes by concentrating on six key changes in your everyday life.

9.1 Practicing good dietery habits

Eating great is significant when you have diabetes, since what you eat influences glucose. No sustenance's are entirely untouchable. Concentrate on eating just as much as body needs. Eat a lot of vegetables, organic products, and entire grains. Pick non-fat dairy and incline meats. Limit nourishments that are high in sugar and fat. Keeping in mind that starches transform into sugar, so limit the carbohydrate consumption. A sound eating routine incorporates the amount we eat as well as what we eat. Here are a few tips which are used in our daily life avoid saturated fat, eliminated nourishments with hydrogenated fats or trans-fat, pick unsaturated, unsaturated fats rather than soaked and trans fats, eat good amount of high-fibre nourishments like entire grain bread, natural products, and vegetables, eat 6 to 8 servings of grains.

9.2 Exercising daily

We do not need to join an exercise center and do broadly educating. Simply walking or doing dynamic computer games are sufficient.

Having a dynamic way of life helps us control our diabetes by cutting down our glucose. It likewise brings down our odds of getting coronary illness (Gupta *et al*., 2008). It can help us lose additional pounds and straight forwardness stress. Our objective might to be 30 min of movement that makes us sweat and inhale somewhat harder most days of the week .

9.3 Getting check-up's

In case if not getting consistent check-ups, atleast now an ideal opportunity to begin. Diabetes raises our danger of coronary illness. It is advised to check cholesterol, pulse, and HbA1C (normal glucose more than 3 months).

9.4 Overlooking stress

When we are focused on, our glucose levels go up. Furthermore, when we are on edge, we may not deal with our diabetes well. We may neglect to work out, eat right, or take our endorsed drugs. It is advised to soothe stress through profound breathing, yoga, or side interests that unwind us.

9.5 Quitting smoking

Diabetes raises our odds of having wellbeing issues like coronary illness, eye malady, stroke, kidney sickness, vein infection, nerve harm, and foot issues. In the event that we smoke, our possibility of getting these issues is much more prominent. Smoking likewise can make it harder to work out.

9.6 Avoiding alcohol

Avoiding excess alcohol may make it easier to control our blood sugar, so if choose to drink, not to overdo it. Drinking alcohol can make our blood sugar go too high or too low.

10. Diabetes mellitus and risk factors

Type 2 diabetes is linked to impaired glucose tolerance due to insulin resistance; concomitant islet beta-cells injury may lead to insulin deficiency which impact on utilization of glucose by skeletal muscle, liver and adipose tissues. Therefore, impaired glucose tolerance coupled with other factors such as genetic disposition, environmental factor, diet, physical inactivity and obesity do significantly contribute to the progression of insulin resistance and to the development of type 2 diabetes.

10.1 Obesity

The increase in the prevalence of obesity has led to increase in the incidence and prevalence has been shown to be linked to increased release of adipocyte-derived bioactive metabolites like lipids, free fatty acids, monocyte chemo attractant protein-1 and pro-inflammatory cytokines. Research indicates that exposure of muscle cells to fatty acids impair insulin-mediated glucose uptake and consequently contribute to insulin resistance and insulin resistance in turn contribute to the development of type 2 diabetes. To justify the possible contributory role of obesity to the development of insulin resistance and in turn in the development of type 2 diabetes, a study on young insulin-resistant lean children of type 2 diabetic individuals and insulin-sensitive controls of similar body mass index, revealed that in lean people, systemic inflammation may not play an important role in the development of insulin resistance. However, human and animal models showed that tumour necrosis factor-alpha gene expression is up-regulated in adipose tissues, therefore linking it to proinflammatory cytokines released from adipose tissues to insulin resistance in type 2 diabetes mellitus.

10.2 Lifestyle

Food intake has been strongly related to obesity in terms of quantity of food, composition and quality. High intake of red meat, sweets and fried food has been reported to contribute to increased risk for the development of insulin resistance and type 2 diabetes while intake of vegetables and fruits has been linked to reduced incidence of type 2 diabetes. In 500 school children who consumed carbonated drinks for a selected period of time, the result indicated that serving additional carbonated drinks increased the incidence of obesity and there is a report of a positive association between intake of sugars and the development of type 2 diabetes. A study in Japan linked the consumption of white rice to increased risk of developing type 2 diabetes supporting the evidence of the association between diet and the risk of developing type 2 diabetes

Physical inactivity is an important mortality risk factor in the development of type 2 diabetes with an increase of 20-30% of death compared with individuals who participate in at least 30 min of daily exercise. Physical activity is reported to be linked to a significant decline in the risk of developing type 2 diabetes. This is because physical activity is believed to increase insulin sensitivity and is reported to be more beneficial in preventing the progression of type 2 diabetes during the initial stage prior to the application of insulin therapy (Soumya Singh *et al*., 2022). During physical activity, contracting skeletal muscle enhances glucose uptake into the cells; physical activity also increases blood flow in the muscle and promotes glucose transport into the muscle cells and physical activity has been reported to decrease intra-abdominal fat-a major risk factor for insulin resistance and in turn for the development of type 2 diabetes. Report shows that there is a 20% increase risk of developing type 2 diabetes for daily increased watching of television for 2 h.

11. Role of herbal remedy in diabetes mellitus treatment

Treatment of diabetes mellitus without any adverse effects is still the biggest question to medical practioners. According to world ethanobotanical, 800 medicinal plants are used for the prevention of diabetes mellitus. Clinically proven that only 450 medicinal plants possess antidiabetic properties from which 109 medicinal plants have complete mode of action. In ancient time, doctor and lay person used traditional medicinal plants with their active constituents and properties for the treatment of various diseases such as heart diseases, cancer and diabetes. There is a long history of traditional plants used for the control of diabetes in India and China. There are various books available such as Charaka Samhita and Susruta Samhita which explains phytopharmacology features of diabetes and its adverse effect. Synthetic drugs which are used for treatment of diabetes are associated with various adverse effect such as sickness, vomiting, dysentery, alcohol flush, migraine, swelling, malignant anemia and faintness. Herbal drugs are proved to be a better choice over synthetic drugs because of less side effects and adverse effects. Herbal formulations are easily available without prescription. These herbal drugs are used for life threatening disease. These drugs are also used when chemical drugs are ineffective in treatment of disease. These are natural and safe drugs, *i.e.,* there is no toxic effects. Herbal drugs permanently cure person and treat the disease while synthetic drugs are not permanently cured the diseases. Herbal formulations contain

natural herbs and fruits and vegetables extract which are beneficial in treatment of various diseases without any adverse effects. On after-hand chemical drugs are prepared synthetically and have side effects. Herbal formulations are cheap as compared to allopathic medicines. Herbal formulations are ecofriendly. Herbal formulations are produced from natural products while allopathic medicines are produced from chemical and chemically modified natural products. Herbal formulations are available without prescription while allopathic medicines are available with prescription.

11.1 The challenges of herbal medicines in India

Although, the medicinal value of herbs, there are some levelled against it; such as need of consistency, specific amount of medicine is not prescribed to patients, dose not strictly given on time, since the manufacturing method is not standardized, varying amounts of the active ingredient are present. Now, the problem is "how to prepare these herbal drugs to clear the above criticisms to struggle with pharmaceutical medicines". It will involve thorough research involving separation and categorization of active constituents of medicinal plants. Also, the herbal drugs and even the conventional medicine currently in use essentially not resulted to cure many diseases. There is need to investigate the alternative therapeutic treatment through study of the plant kingdom and rationale of their potentials through relative studies.

11.2 The future aspects of herbal remedies for diabetes mellitus

Many herbal drugs are used by people and various native drugs are regularly being introduced into current therapeutics. About 80% of the people, in developing countries particularly the rural people, rely on the conventional medical remedies for health care requirements. There has been a revival of interest in herbal drugs in developed countries due to a huge amount on the preference of products from natural sources. Therefore, there is a need to differentiate between herbal drugs supplied by a medical practitioner and those herbal remedies easily accessible to the people for self medication. The rapidly growing occurrence of diabetes mellitus is a seriousness to human physical condition in all over the world. Recently, new active medicines have been extracted from plants and possess anti-diabetic activity with more effectiveness than oral hypoglycemic agents used in proven therapy. In recent years, awareness has been drawn towards discovery of plants with antidiabetic activity that may be useful to people. It may also provide evidence for the improvement of a new oral drug for the treatment of diabetes mellitus (Asha Arora *et al*., 2022).

12. Conclusion

Diabetes mellitus is a most common endocrine disorder, affecting millions of people worldwide. It is a group of metabolic diseases characterized by hyperglycemia resulting from defects in insulin secretion, insulin action, or both. The increase in resistance and populations of patients at some risk, in conjunction with the restricted number of commercially available drugs for diabetes that still present have many side effects and also problems like unwanted hypoglycemic effect are the cause to shift the research towards traditionally available medicine which have low side effect and wide range of bioactivity and do not require laborious pharmaceutical synthesis seems highly attractive.

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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