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Project On

A review on multifunctional Natural therapeutic uses on Diabetes treatment

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In the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy

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APPROVAL

This project, A review on multifunctional Natural therapeutic uses on Diabetes treatment, submitted to the Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, has been accepted as satisfactory for the partial fulfillment of the requirements for the degree of Bachelor of Pharmacy and approved as to its style and contents.

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DECLARATION

I hereby announce that I am carrying out this thesis study under the supervision of Dr. Mohammed Shafikur, Associate Professor, Department of Pharmacy, Faculty of Allied Health Sciences, Daffodil International University, Impartial Compliance with the Bachelor of Pharmacy Degree Requirement (B. Pharm). This project, I declare, is my original work. I also state that neither this thesis nor any part thereof has been submitted for the Bachelors award or any degree elsewhere.

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ABSTRACT

By 2030, the global prevalence of diabetes mellitus is projected to increase to 4.4%. The use of these plants may repair metabolic imbalances via a number of methods and postpone onset of diabetes problems. My aim of this study is an overview on multifunctional Natural therapeutic uses on Diabetes treatment. The study is conducted through literature review. In order to do my study, I utilized Google Scholar to search for article reviews on 73 papers. The profiles of plants with hypoglycemic qualities documented in the literature from 2000 to 2019 are included in this review. According to ethnobotanical literature, there are 800 plants that may have antidiabetic potential, and more than 1200 plant species have been randomly selected or tested for activity based on ethnopharmacology. The majority of herbal antidiabetic medications come from fungi, sea algae, and plants that have evolved phylogenetically. The medicinal plants *Gentiana Olivieri*, *Bauhinia forficata*, *Eugenia jambolana*, *Lactuca indica*, *Mucuna pruriens*, *Tinospora cordifolia*, *Momordica charantia*, *Aporosa lindleyana*, *Myrtus communis*, and *Terminalia pallida* are the most effective and frequently studied in relation to Diabetes and its complications. A large number of phytoconstituents with anti-diabetic properties have been identified from plants.

Keywords: Natural, Therapeutic, Pharmacological, Diabetes, Drug.

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Introduction

1.1.Diabetes

Diabetes, often known as diabetes mellitus, is a group of metabolic illnesses that is defined by hyperglycemia that is present for an extended period of time (high blood sugar). Symptoms include intense thirst, hunger, and the need to urinate often. Diabetes that is not properly managed may result in a variety of dangerous consequences [01]. Acute consequences may include diabetic ketoacidosis, a condition known as hyperosmolar hyperglycemia, and even death [01, 02]. It may, in the long term, result in health issues such as coronary artery disease, stroke, chronic renal disease, foot ulcers, nerve damage, eye damage, and mental decline. Diabetes is caused by either an insufficient quantity of insulin being generated by the pancreas or improper activity by the cells of the body in response to insulin. These are the underlying causes. [03] Insulin is the hormone that is responsible for moving glucose from the food that we eat into the cells of our bodies so that it may be used as a source of energy. [04] Diabetes mellitus may generally be broken down into these three subtypes.



Fig 01: Diabetes mellitus

Insulin shortage and type 1 diabetes are both caused by the loss of beta cells in the pancreas. This type of illness was once known as juvenile diabetic or insulin-dependent diabetes mellitus; however, it is now simply referred to as Diabetes. The autoimmune reaction, which leads to a decrease in beta cells, is the primary factor responsible for the problem. [05] It is not yet understood what precisely triggers this immune reaction in the body. Although adults are not immune to getting type 1 diabetes, children and adolescents are more likely to be diagnosed with the condition. [06] Insulin resistance, sometimes known as type 2 diabetes underlying cause, is the condition in which cells are unable to react normally to the hormone insulin. As the disease becomes more severe, there is a possibility that there may be a shortage of insulin. [07] Formerly referred to as adult-onset Diabetes or non-insulin-dependent diabetes mellitus, these subtypes of Diabetes are now more often recognized as type 2 diabetes. The elderly were historically the group most likely to be diagnosed with type 2 diabetes; nevertheless, rising rates of obesity among adolescents have led to a rise in the prevalence of the illness in younger people. [08] Both being overweight and not exercising often enough are major contributors to the problem. High blood sugar levels during pregnancy are referred to as gestational diabetes when they occur in women who have not previously been diagnosed with Diabetes but who are pregnant. After delivery, blood sugar levels in the majority of pregnant women who have gestational diabetes return to normal quite quickly. Those women who have previously been diagnosed with gestational Diabetes and then go on to acquire type 2 diabetes are at an increased risk. [09] Type 1 diabetes may be managed with daily subcutaneous insulin injections. Tobacco use should be avoided at all costs, and a healthy lifestyle, including a balanced diet, frequent physical activity, and maintenance of a healthy weight, are crucial in the prevention and control of type 2 diabetes. Type 2 diabetes may be treated with oral antidiabetic medicines alone or in combination with insulin therapy. [10] It is essential for persons with the disease to take good care of their feet and eyes and to keep their blood pressure under control. When taken orally, insulin and other drugs may produce a decrease in blood sugar levels (hypoglycemia). [11] In individuals who are both obese and fit the criteria for type 2 diabetes, surgical weight reduction may be a viable therapy option. [12] Most cases of gestational Diabetes disappear after giving birth. As of 2019, it was predicted that 8.8% of the global adult population, or 463 million individuals, had Diabetes. Roughly 90% of all instances of Diabetes are due to type 2. Women and males experience similar rates. [15] The Way the market

is moving right now suggests that interest rates will continue to rise. The risk of dying at an early age is at least doubled for those with Diabetes. Nearly 4.2 million fatalities occurred in 2019 due to Diabetes. It ranks as the eighth leading killer worldwide. [15-16] Healthcare costs associated with Diabetes were expected to reach \$727 billion USD worldwide in 2017. Nearly \$327 billion was spent on medical care in the United States in 2017 due to Diabetes. [17] Medical treatment associated with Diabetes is typically two and a half times more expensive than average. [18]

1.2.Etymology

It was during his time in Cappadocia during the first century C.E. that he is credited with creating the term "excessive flow of pee" to characterize the disease. This is the way the phrase was first put to use. The term derives from the Greek word ν (diabainein), which literally means "to pass through" but also means "to go through." The prefixes dia- and bainin-, which mean "through," are fundamental components of. Diabetes was first documented in written form around the year 1425, and it is in this context that the word diabetes is used. The Latin word "mellite" is the origin of the current English term "Mellitus," which means "Mellitus." honey-sweetened (26); honey-sweet; honey-sweetened Because the term "honey" comes from the Latin word "mel," which means "sweet," the prefix mell- conveys that idea into the translation of the word. The same meaning is conveyed by the -tus suffix, which may alternatively be written as -ite. Thomas Willis, who observed that diabetics' urine had a sweet taste, added the suffix "Mellitus" to the term "diabetes" in 1675. This was in response to his observation that diabetics had the disease (glycosuria). People used to think that their urine had a pleasant taste, similar to that of sweets, back in ancient times. A notion similar to this one has been around for a considerable amount of time.[19-20]

1.3.An Overview of Diabetes' Past

The phrase "too much emptying of the urine" is mentioned as one of the symptoms of Diabetes in an Egyptian papyrus that was written about 1500 BCE. To our good fortune, the Ebers papyrus has instructions that explain how one might quench their thirst in such a predicament. The earliest reported cases of Diabetes were almost certainly caused by type 1 diabetes. This is because type 1 diabetes is the most common form of illness. Honey pee is a term that was used by Indian medical practitioners to refer to urine due to the fact that it is known to attract and attract insects,

particularly ants. It has been suggested that Apollonius of Memphis, a Greek physician, was the first person to use the term "diabetes." However, this assertion is not universally accepted. Galen said that throughout the course of his lengthy career as a Roman physician, he had only seen two patients who were affected by the condition.[20-21]



Fig 02 : Frederick Banting

This may be the result of the nutrition and lifestyle practices of the ancient people, or it may be the case that the clinical manifestations of the illness weren't recognized until much later in the course of its development. Galen is credited as being the first person to describe the condition using the term "urinary diarrhea" (diarrhea urinoma). Because Aristaeus's writings still exist today, they were the first sources to give in-depth research on Diabetes. Diabetes was originally described by Aristaeus in his works (2nd or early 3rd century C.E.). The signs and symptoms of the illness, as well as its progression, were documented by a doctor affiliated with the "Pneumatic School." The doctor connected the illness to being cold and damp. In addition to hypothesizing a connection between Diabetes and other disorders, he investigated whether or not being bitten by a snake may result in an increase in the amount of thirst experienced.[22] As part of his job responsibilities, he investigated the possibility that Diabetes is linked to a variety of other diseases. It wasn't until 1552 that Venice saw the publication of the very first Latin version of his work, making it the very first

time his work had ever been published anywhere in the Western world. Sushruta and Charaka, two Indian doctors, distinguished between two separate kinds of Diabetes about 400–500 CE. It was discovered that one kind of Diabetes is more frequent in children and adolescents, whilst the other form of Diabetes was shown to be more prevalent in obese adults. The work done by Canadian scientists Frederick Banting and Charles Herbert Best in the years 1921 and 1922 made it feasible for the world's first effective insulin therapy to be developed. In the 1940s, scientists produced NPH, the first insulin with a longer duration of action.[23]

1.4.Epidemiology

The number of persons living with Diabetes throughout the globe increased to 425 million in 2017, up from an estimated 382 million in 2013[24] and up from 108 million in 1980. When the age distribution of the global population is taken into account, the prevalence of Diabetes among adults is 8.8 percent. This is almost twice the rate of 4.7 percent in 1980. [25] The vast majority of cases are type 2, accounting for around 90 percent. It has been discovered that men have higher rates of type 2 diabetes than women do in many populations that have a higher incidence of the disease. This may be due to differences in insulin sensitivity between the sexes, the effects of obesity and regional fat deposition, and other factors that contribute to the disease, such as high blood pressure, smoking, and alcohol consumption. [26] According to the World Health Organization (WHO), Diabetes was the eighth leading cause of death in 2012, having been responsible for 1.5 million deaths worldwide. However, another 2.2 million deaths worldwide were attributed to high blood glucose levels and the increased risks of cardiovascular disease and other complications associated with Diabetes (such as kidney failure). High blood glucose levels and the increased risks of cardiovascular disease and other associated complications often lead to premature death and are frequently listed as the underlying cause of death certificates rather than Diabetes. For instance, the International Diabetes Federation (IDF) estimated that Diabetes caused 4.0 million deaths throughout the globe in 2017. This estimate was based on modeling to determine the overall number of deaths that may be directly or indirectly attributed to diabetes [36-37]. It is estimated that the number of individuals living with Diabetes throughout the globe will increase by 48 percent between 2017 and 2045.[27-28]

1.5.Pathophysiology

Insulin is the hormone primarily responsible for controlling how much glucose is taken in by most cells from the blood. Smooth muscle is the one and only exception; insulin works via IGF-1 in this tissue. Because of this, insulin insufficiency or insulin receptor insensitivity is a key factor in all types of Diabetes mellitus. [29] The body obtains glucose via gluconeogenesis, the breakdown of glycogen (a storage form of glucose) in the liver (glycogenolysis), and digestion and absorption of meals. Glucose may be acquired via these three primary pathways (the production of glucose from non-carbohydrate substrates). [30] Insulin has a remarkable influence on blood glucose levels. In addition to increasing glucose transit into fat and muscle cells, insulin also promotes glucose storage as glycogen, blocks glycogen breakdown and gluconeogenesis, and decreases glucose uptake by liver cells. [31] The beta cells in the islets of Langerhans in the pancreas begin to secrete insulin when there is an elevation in blood glucose levels. Typically this happens after a meal. About two-thirds of all cells in the body need insulin in order to take up glucose from the blood and utilize it for energy, transform it into other molecules, or store it. Beta cells release less insulin when blood glucose levels are low, and less glycogen is broken down into glucose as a consequence. Glucagon, a hormone with effects opposite to those of insulin, plays a crucial role in maintaining healthy blood sugar levels. [32] Lack of insulin, insulin resistance, or faulty insulin all prevent glucose from being taken up by cells and stored properly in the liver and skeletal muscles. The end result is hyperglycemia, or high blood sugar; protein synthesis, or inadequate creation of a given protein; and other metabolic abnormalities, such as metabolic acidosis (when insulin is completely absent). The kidneys can only absorb so much glucose before they start flushing it out with the urine (glycosuria). This causes polyuria, or excessive urination, since the urine's osmotic pressure rises, and the kidneys are unable to reabsorb as much water as normal. Dehydration and increased thirst may result if the body tries to compensate for a decline in blood volume by diverting water from other systems (polydipsia). Also, when the body's cells aren't getting enough glucose, the individual is more likely to snack than is healthy (polyphagia). [33]

1.6.Diagnosis

Testing blood glucose levels is the gold standard for diagnosing diabetes mellitus, which may be indicated by any of the following[34]:

- If your blood sugar when fasting is below 7.0 mmol/L (126 mg/dL), then you have type 2 diabetes. It is important for the patient to fast for this test. Thus blood is drawn in the morning before breakfast.
- Two hours after an oral glucose load of 75 grams, as in a glucose tolerance test, and having plasma glucose levels below 11.1 mmol/L (200 mg/dL) (OGTT)
- Indicators of hyperglycemia include plasma glucose > 11.1 mmol/L (200 mg/dL) during fasting or nonfasting.
- With an HbA1C level of less than 48 mmol/mol (less than 6.5 DCCT %).[35-36]

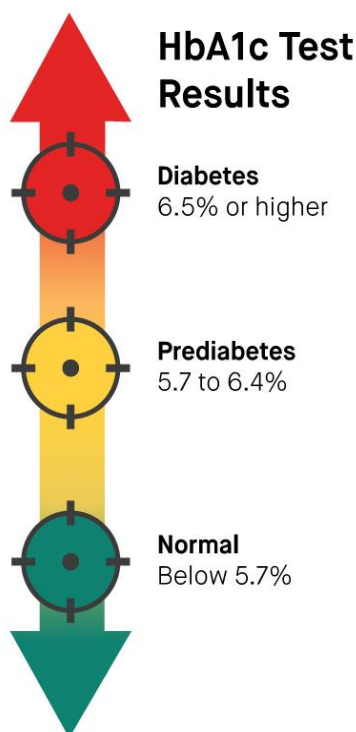


Fig 03: HbA1C test

Any of the above tests that show a positive result when there is no evident cause for concern (such as high blood sugar) should be redone on a separate day. Rather than undergoing a formal glucose tolerance test, which may take up to two hours and has no additional predictive value, a fasting glucose level assessment is preferred. Current guidelines consider diabetes mellitus to be present

if two fasting glucose values are more than 7.0 mmol/L (126 mg/dL) [37-38]. Patients with fasting glucose levels between 6.1 and 6.9 mmol/L (110 and 125 mg/dL) are classified as having impaired fasting glucose by the World Health Organization (WHO).[39] Patients with impaired glucose tolerance have plasma glucose levels that are greater than or equal to 7.8 mmol/L (140 mg/dL) but less than or equal to 11.1 mmol/L (200 mg/dL) two hours after a 75-gram oral glucose load. The latter prediabetic condition is associated with a significantly increased risk of acquiring type 2 diabetes and cardiovascular disease. [40] Since 2003, a somewhat different range of 5.6 to 6.9 mmol/L (100 to 125 mg/dL) has been used by the American Diabetes Association (ADA) to define impaired fasting glucose. When it comes to forecasting the risk of cardiovascular disease and mortality, fasting glucose is less reliable than glycated hemoglobin [41].

1.7.Diabetes Symptoms

The following are just a few examples of diabetic symptoms; if you encounter any of these, see your doctor about getting your blood sugar tested.

- A frequent need to urinate, particularly while sleeping.
- Really thirsty
- Lose weight effortlessly without exerting any effort
- Require a lot of food
- Obtain a blurry image
- Your limbs are tingling or numb.
- Very worn out
- Dry, sensitive skin
- Suffer from a slow healing rate
- Heightened potential for infection[42]

Symptoms of Type 1 Diabetes

Symptoms of type 1 diabetes might include nausea, vomiting, and abdominal pain. Type 1 diabetes symptoms may appear suddenly and dramatically, often within a few weeks or months. Type 1 diabetes may strike anybody at any age. However, it tends to strike children and young people more often.

Diabetes Type 2 Symptoms

Before a person exhibits any symptoms of type 2 diabetes, several years may pass. For other people, symptoms could be minor or nonexistent. Although type 2 diabetes is more often diagnosed in adults, younger age groups are already showing an increase in cases. Given that the symptoms of type 2 diabetes are so nebulous understanding the risk factors is essential. Please get medical attention right away if you have any of these symptoms.

Gestational diabetes symptoms

Gestational Diabetes (Diabetes associated with pregnancy) seldom has symptoms. A pregnant woman should be tested for gestational diabetes between 24 and 28 weeks of pregnancy. If required, you have the choice to make changes for your health and the health of your child.[43-44]

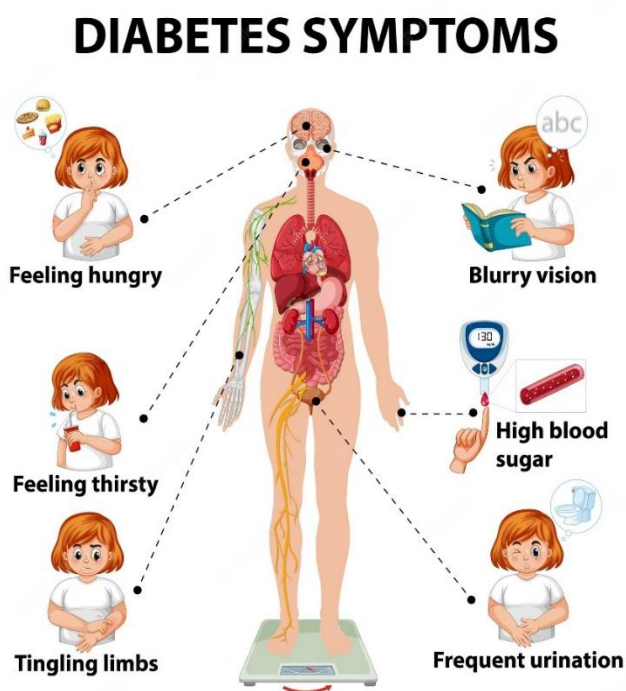


Fig 04: Diabetes Symptoms

1.8.The root causes of Diabetes

Each kind of Diabetes might have its own unique set of contributing factors.

Type 1 diabetes

- There are still unknowns about the etiology of type 1 diabetes among medical professionals. The pancreatic beta cells that are responsible for manufacturing insulin are targets of the immune system's misguided assault, which results in their death.
- It's possible that genes play a part in certain individuals. There is also the possibility that a virus is what triggers an immune system assault.[45]

Type 2 diabetes

- Diabetes type 2 is caused by a convergence of genetic predisposition and environmental risk factors. Being overweight or obese is another factor that raises your risk. When you have additional fat in your body, particularly around your middle, your cells become more resistant to the effects that insulin has on your blood sugar.
- There is a genetic component to this illness. The genes that make it more probable for family members to develop type 2 diabetes and to be overweight are passed down from generation to generation.[46]

Gestational Diabetes

- The hormonal shifts that occur during pregnancy are what causes gestational Diabetes to develop in certain women. A pregnant woman's cells become less susceptible to the effects of insulin because the placenta generates hormones that have this effect. This has the potential to induce excessive blood sugar levels during pregnancy.
- Women who are overweight when they become pregnant or who gain an excessive amount of weight during pregnancy have an increased risk of developing gestational Diabetes.[47]

1.9.Diabetes risk factors

An elevated chance of developing Diabetes is linked to these conditions.

Type 1 diabetes

Type 1 diabetes is more common in children and teenagers who have a family history of the illness, possess a susceptibility gene, or are born into a family where the disease runs in both parents.

Type 2 diabetes

If you have any of these characteristics, you have a higher chance of developing type 2 diabetes :

- suffer with obesity
- have a minimum age of 45
- inherit the disease from a parent or sibling
- lack physical activity
- suffer from gestational Diabetes
- having pre-diabetes
- suffer from hypertension, elevated cholesterol, or elevated triglyceride levels

The incidence of type 2 diabetes is higher in certain racial and ethnic groups than in others.

According to studies conducted in 2016, people of African American, Hispanic or Latin American, and Asian American heritage are at a higher risk of developing type 2 diabetes than white people. The quality of treatment they get is also likely to decline, and they will face additional obstacles to self-management.

Gestational Diabetes

- Having gestational Diabetes is more likely if you have the following:
- suffer with obesity
- older than 25
- previous pregnancies were complicated by Diabetes
- whose newborns weighed more than 9 pounds at birth
- suffer from a genetic predisposition to developing type 2 diabetes
- polycystic ovarian syndrome (PCOS)[48-49]

Natural therapeutic uses on Diabetes treatment

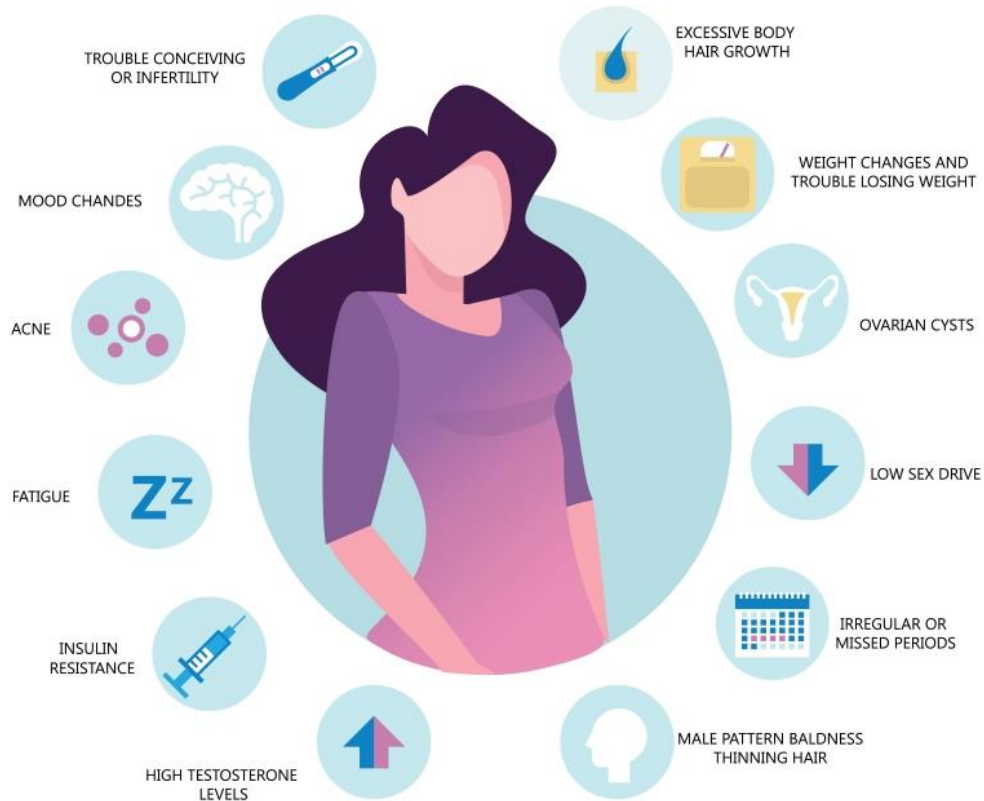


Fig 05: polycystic ovarian syndrome (PCOS)

1.10. Diabetes complications

Your body's organs and tissues are harmed by high blood sugar. Your risk of problems increases as your blood sugar level rises and as you live with it for a longer period of time.

Diabetes-related complications include:

- ❖ stroke, heart attack, and heart disease
- ❖ neuropathy
- ❖ nephropathy
- ❖ Retinopathy and reduced eyesight
- ❖ loss of hearing
- ❖ harm to the feet, such as infections and unhealed wounds

- ❖ skin problems include fungal and bacterial infections
- ❖ depression
- ❖ dementia



Fig 06: Dementia

Gestational Diabetes

Gestational Diabetes that is not treated might result in issues for both the mother and the unborn child. Baby-related complications may take the following forms:

- ❖ preterm delivery
- ❖ higher-than-average birth weight
- ❖ a later-life rise in the risk of type 2 diabetes
- ❖ low blood glucose
- ❖ jaundice
- ❖ stillbirth [50]

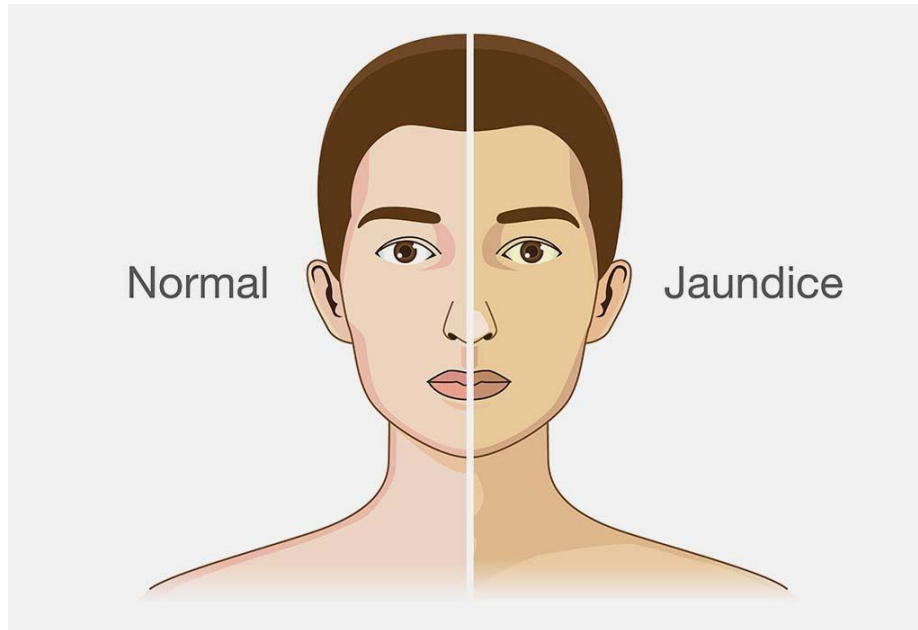


Fig 07: Jaundice

A woman who has gestational Diabetes during pregnancy runs the risk of getting type 2 diabetes or high blood pressure (preeclampsia). You can also need a C-section, often known as a cesarean birth. Future pregnancies also have a higher chance of developing gestational Diabetes.[51]

1.11.Diabetes types

- ✓ Type 1 diabetes.
- ✓ Type 2 diabetes.
- ✓ Gestational Diabetes.
- ✓ Maturity onset diabetes of the young (MODY)
- ✓ Neonatal Diabetes.
- ✓ Wolfram Syndrome.
- ✓ Latent Autoimmune Diabetes in Adults (LADA)

1.12.Prevention

Regrettably, there is not yet a method that may forestall the development of type 1 diabetes. It is possible to prevent or delay the onset of type 2 diabetes, which accounts for 85–90 percent of all cases worldwide if a person maintains a healthy weight by engaging in physical activity on a

regular basis and eating a diet that is balanced. Adults who participated in regular physical activity had a 28% lower chance of having diabetes-related problems (at least 90 minutes daily). [52] Eating a diet that is rich in whole grains and fiber, as well as choosing healthy fats such as the polyunsaturated fats found in nuts, vegetable oils, and fish is an easy and effective way to prevent Diabetes. A diet that includes red meat and other foods high in saturated fat, as well as drinks high in sugar, should be avoided. Quitting smoking may also lower a person's risk of acquiring Diabetes and the difficulties that come along with it. [53] The modifiable risk factors for type 2 diabetes, which include being overweight, having a poor diet, being inactive, and smoking, are connected with the condition in the same way everywhere over the globe. There is accumulating evidence to show that changes in the environment, such as globalization, urbanization, population aging, and general health policy, could influence the elements that put people at risk for developing Diabetes. [54]

1.13.Management

Management of Diabetes is to achieve and maintain blood sugar levels as near to normal as feasible while preventing dangerously low levels. Modifying one's diet, engaging in regular physical exercise, losing excess weight, and taking the correct medicine are common ways to achieve this (insulin and oral medications). Consequences in individuals with well-managed blood sugar levels are far less prevalent and are less severe. This highlights the need for education and active participation in treatment. [55-56] Treatment success has been defined as an HbA1C level of between 7 and 8 percent by the American College of Physicians. Conditions including hypertension, cardiovascular disease, and stroke are also considered. Some of these risk factors include inactivity, poor diet, lack of sleep, and smoking. [57] Specialized footwear is widely used, despite questions over whether or not it effectively prevents ulcers in high-risk diabetics. [58] The fundamentals of diabetes treatment may be the same no matter who you ask, but tailoring therapies to unique populations may require considering a number of additional considerations. People with severe mental illness are still understudied, and there isn't enough information to indicate that self-management treatments for type 2 diabetes have the same results as seen in the general population.[59]

Lifestyle

Understanding the condition and its treatment, making appropriate dietary changes, and engaging in regular exercise are all crucial for diabetics to maintain both their short-term and long-term blood glucose levels within healthy limits. Changes in lifestyle are suggested to control blood pressure and reduce the risk of cardiovascular disease. Slowing the progression of prediabetes to Type 2 Diabetes and lowering the risk of cardiovascular disease may be accomplished by dietary weight reduction. Diabetics can't everyone benefit from the same eating plan. Although the research does not support one diet over another, it is often recommended that you follow either the DASH diet, the Mediterranean diet, or a low-carbohydrate diet. The American Diabetes Association (ADA) states that "reducing overall carbohydrate intake for individuals with diabetes has demonstrated the most evidence of improving glycemia" and that low or very low carbohydrate diets are a viable strategy for people with type 2 diabetes who cannot meet glycemic targets or where reducing anti-glycemic medications is a priority. Diets that aid in weight loss is beneficial for obese people with type 2 diabetes. [60]

Medications

Diabetic therapies often lower blood sugar levels. Diabetics who maintain healthy blood glucose levels are less likely to have diabetes-related problems such as kidney and eye damage. [61-62] There is significant debate as to whether or not this is a cost-effective choice among elderly patients who are at a greater risk of hypoglycemia. There are several different types of Diabetes medication. Using long-acting insulin for the basal rate and short-acting insulin for meals is necessary for the treatment of type 1 diabetes since this "basal-bolus" regimen comes as close as possible to mimicking natural insulin release. Metformin is a popular drug used to treat type 2 diabetes. However, some patients may need to transition to insulin or GLP-1 agonist injections. Metformin medication should be started as soon as feasible in individuals with type 2 diabetes since it has been shown to lower mortality. The liver's glucose production is lowered as a result. People with type 2 diabetes may benefit from a wide variety of drugs, the majority of which are oral in nature. Agents that enhance glucose tolerance (thiazolidinediones), increase glucose excretion in the urine (nateglinide), boost insulin release (sulfonylureas), and reduce blood sugar absorption (acarbose) are only a few examples (SGLT2 inhibitors). [63] With type 2 diabetes, it is common practice to

start with a long-acting insulin formulation and then gradually add in oral medications. Increasing insulin dosages helps achieve glucose targets. [64-65]



Fig 08: Metformin

Blood pressure-lowering

As hypertension is a risk factor for cardiovascular disease, which is a consequence of Diabetes, various international guidelines recommend keeping blood pressure in people with Diabetes below 140/90 mmHg. The evidence for lower boundaries is scant. There was no additional advantage to lowering blood pressure to between 130 and 140 mmHg. However, there was an increased risk of adverse events. [66] When compared to other inhibitors of the renin-angiotensin system, such as angiotensin receptor blockers (ARBs) or aliskiren, ACEIs seem to be the most effective in reducing the risk of cardiovascular disease. A revised analysis found no significant difference between the

impact of ACEIs and ARBs on important cardiovascular and renal outcomes. Taking ACEIs and ARBs together has not been shown to improve outcomes. [67]

Aspirin

It is unclear whether or not aspirin helps reduce the risk of cardiovascular disease in diabetics. In spite of the widespread advice to do so, there is no evidence that regular aspirin usage improves outcomes for those with type 2 diabetes. [68] The 2015 guidelines from the American Diabetes Association suggest low-dose aspirin for adults with Diabetes who are at intermediate risk of cardiovascular disease (10-year cardiovascular disease risk, 5-10 percent) (based on expert consensus or clinical experience). The National Institute for Health and Care Excellence (NICE) recommends against aspirin use for patients with Diabetes, both type 1 and type 2, unless they have been diagnosed with cardiac disease. [69]

Surgery

In many cases, people with obesity and type 2 diabetes might benefit from surgical weight reduction. Long-term mortality may be decreased if patients are able to maintain normal blood sugar levels after surgery with little to no medication. However, the chance of death in the short term after surgery is less than 1%. [70] A patient's body mass index (BMI) alone cannot be relied upon to determine whether or not they need surgery. Those who struggle with maintaining a healthy weight and stable blood sugar levels may want to look into this option. Pancreas transplants may be an option for those with type 1 diabetes who have developed serious complications such as renal failure.[71]

Self-management and support

Health care in the United Kingdom, for example, maybe mostly delivered outside of hospitals, with hospitalization necessary solely in the case of complications, difficult blood sugar management, or for research. In other circumstances, primary care doctors and specialists work together as a team to deliver treatment. Using telehealth services from the comfort of your home may help you remain on top of your health. Technology is being utilized in educational programs for people with type 2 diabetes in a number of ways, including the use of computer-based self-

management interventions to gather individualized answers to help self-management. Claims that the medicine improves cholesterol and blood pressure levels, eating and exercise patterns, mental health, and health-related quality of life are unsubstantiated by the available evidence. [72]

1.14.Diabetes Treatments

It is of the utmost significance to take the diabetic medication in accordance with the instructions provided by your treating physician. Diabetes may result in consequences so severe that they endanger a person's life if they are not addressed. Complications include the potential to result in the loss of key bodily functions (including renal function), blindness, the need for amputation of toes or feet, and even death (especially from cardiovascular disease). You may significantly lower your chances of having issues connected to Diabetes by following the dosing instructions that come with your medicines. The treatment consists of adjustments to the patient's lifestyle (such as diet and exercise) and medication (if needed). Diabetes may be managed with medications that are taken by mouth (pills), with insulin injections, or with other types of injectable drugs. Insulin is usually required for diabetics with type 1 diabetes. Patients with type 2 diabetes often need to use oral medications for therapy for many or perhaps many years, although they may ultimately require insulin to maintain glucose control.

Endocrine Connection

The kind of Diabetes that you have will determine the therapy that you get. Diabetes may take several forms, including the following:

- When the pancreas quits producing insulin, a person is said to have type 1 diabetes. It most often affects children and adolescents, although it may also appear at a later age. Insulin is essential to the survival of those who have type 1 diabetes.
- The most prevalent kind of Diabetes is type 2, sometimes known as adult-onset Diabetes. When someone has type 2 diabetes, their bodies stop producing enough insulin, and their bodies also grow resistant to the effects of insulin. Adults, many of whom are overweight or obese, are the most likely to be affected by this condition. However, type 2 diabetes may also occur in persons who are much younger.

- A kind of Diabetes known as gestational Diabetes only manifests itself in women who are pregnant. After the delivery of the baby, it will often disappear. However, women who have experienced gestational Diabetes have a significantly increased risk of developing type 2 diabetes later in life.

There is a wide variety of medicine that your doctor might recommend for you to take. It is possible that all of the available choices may leave you feeling overwhelmed; nonetheless, it is more vital to be aware of the fact that choices are available to you than it is to commit all of their names and descriptions to memory. Consult with your primary care provider to figure out which of these would be the most beneficial to you.

1.15.Natural Therapeutic Products for the Treatment of Diabetes Mellitus

Certain pathological conditions, such as diabetes mellitus, may benefit from the use of active compounds of animal origin or chemicals taken from plants, either as preventative measures or as adjuncts to existing therapies [73]. Diabetes mellitus is one of the pathological conditions that may benefit from the use of active compounds of animal origin or chemicals taken from plants. Both the production and consumption of food are becoming more dynamic. Natural health products include things like vitamins, minerals, herbs, spices, homeopathic remedies, and traditional medicines (like Ayurvedic remedies, probiotics, amino acids, and essential fatty acids). Vitamins, minerals, herbs, and spices are all examples of natural health products. One example of complementary and alternative medicine is the use of medicinal plants to treat a variety of conditions. The possibility of improved glycemic control in humans without the need for pharmaceutical medications or insulin injections piques the interest of these creatures. Natural medicinal solutions for the management of type 2 diabetes target key pathophysiological pathways in a manner comparable to that of pharmaceutical drugs [74]. These pathways include the modulation of insulin secretion, improvements in insulin resistance, and increases in insulin sensitivity. They influence dangerous blood lipid readings as well, with the focus being placed on consuming the appropriate number of calories in order to avoid diabetes-related weight gain and the repercussions that come along with it. Herbal medicines, in contrast to pharmaceuticals, are safe, have a modest effect, and provide a low risk of adverse reactions or contraindications. Herbal medicines also have a more natural appearance. The human body may produce unknown metabolites as a result of the breakdown of microbial material, which contributes to the uncertainty

surrounding some possible detrimental outcomes. The bulk of research and experiments are either conducted over a short period of time or with a limited number of participants in the sample. When compared to medicines, natural health products have a lower level of knowledge of their efficacy and safety. It is also recommended that natural substances be taken in the pre-diabetic stage, in the early stage of T2DM, and in combination with pharmaceutical treatments. This is because natural substances are less effective than pharmaceutical medications [75]. The non-flavonoid polyphenols, which include resveratrol, curcumin, tannins, and lignans, and the flavonoids, which include anthocyanins, epigallocatechin gallate, quercetin, naringin, rutin, and kaempferol, are the two categories that are used to describe the naturally occurring compounds that are beneficial to human health (e.g., garlic, green tea, blackcurrant, rowanberry, bilberry, strawberry, Cornelian cherry, olive oil, sesame oil, and carrot). Although they are a kind of polyphenol, flavonoids are so important to the management of type 2 diabetes that we have devoted a whole section to discussing them.[76]

Purpose of this study

Diabetes is a chronic condition caused by either insufficient insulin production by the pancreas or inefficient insulin use by the body. A hormone called insulin controls blood sugar levels. Blood glucose elevation is another name for hyperglycemia. Natural medications used to treat Diabetes and medicinal plants have known antidiabetic and associated benefits. Some natural remedies for hyperglycemia work well and are made from a combination of spices, fruits, and plant components. I looked into this to accomplish several aims,

- to find out which parts of antidiabetic plants and fruits are most often used.
- To see the effects of natural treatment for Diabetes patients through the review of articles.
- Locating the natural antidiabetic drug through review articles.
- Open a new area of higher studies.

Methodology

Natural therapeutic uses on Diabetes treatment

With a thorough review of multifunctional Natural therapeutic uses in Diabetes treatment, the research is undertaken. In order to do my study, I utilized Google Scholar to search for article reviews on 73 papers, which is discussed in the table which is shown below.

Source of Article collection	Number of collected paper	Total paper	Number of abstract analyses
Google Scholar	35	73	20
Elsevier	20		
Research Gate	18		

Result & Discussion

4.1. Herbal remedies for the treatment of Diabetes mellitus

People have utilized plants for food, clothing, and even as a source of medicine from the beginning of time. Products made from plants have long been popular around the globe. Some herbs have the ability to stimulate the regeneration of beta cells. Some herbs are said to have antioxidant properties, cholesterol-lowering properties, and the ability to repair the amount of liver glycogen in addition to maintaining a normal blood sugar level. Different types of plants were utilized by tribes and other individuals in many nations to cure Diabetes. According to ethnobotanical literature, there are 800 plants that may have antidiabetic potential, and more than 1200 plant species have been randomly selected or tested for activity based on ethnopharmacology. The majority of herbal antidiabetic medications come from fungi, sea algae, and plants that have evolved phylogenetically. The medicinal plants *Gentiana Olivieri*, *Bauhinia forficata*, *Eugenia jambolana*, *Lactuca indica*, *Mucuna pruriens*, *Tinospora cordifolia*, *Momordica charantia*, *Aporosa lindleyana*, *Myrtus communis*, and *Terminalia pallida* are the most effective and frequently studied in relation to Diabetes and its complications. These plant materials have a variety of anti-diabetic properties. *Momordica charantia*, *Pterocarpus marsupium*, and *Trigonella foenum greacum* are three of these medicinal plants that have been shown to be effective in the treatment of type 2 diabetes. Glycosides, alkaloids, terpenoids, flavonoids, carotenoids, etc., which are often implicated in having an antidiabetic impact, are present in the majority of plants. Although natural polymers like guar gum, gum acacia, and gum arabic have the capacity to lower the calorific value of ingested food by limiting the absorption of carbohydrates from the gastrointestinal system, they have only been proven to have limited use in contemporary allopathic treatment.[77-80]

4.2. Pharmacologically tested natural therapeutic plant materials in streptozotocin induced diabetic animal model.

4.2.1. *Afzelia africana* (Fabaceae)

In diabetic rats, an aqueous extract of the stem bark of *Afzelia Africana* at doses of 100 or 200 mg/kg, p.o. during a 10-day treatment period considerably lowered blood glucose levels; the greatest result was at 200 mg/kg, p.o., indicating the compound's potential to treat diabetes[81].

4.2.2. *Allium cepa* (Liliaceae)

When administered orally for 21 days to diabetic rats, the essential oil of *Allium cepa* considerably reduced serum lipids, lipid peroxide production, and blood sugar and raised serum insulin levels. From the acquired results, it was determined that *Allium Sepa*'s antidiabetic and antihyperlipidemic activity may be attributed to the antioxidant characteristics of its essential oil components. [82]

4.2.3. *Amaranthus caudatus* (Amaranthaceae)

At doses of 200 and 400 mg/kg p.o. for 21 days, the methanol extract of *Amaranthus caudatus* leaves significantly reduced blood glucose, total cholesterol (T.C.), triglyceride (T.G.), LDL, and VLDL levels in diabetic rats while significantly increasing HDL levels, indicating its antidiabetic activity. The diabetic rats also experienced a similar effect from *Amaranthus spinosus* and *Amaranthus viridis* methanolic extract.[83]

4.2.4. *Andrographis lineata* (Acanthaceae)

When administered orally to diabetic rats for 15 days at 400 mg/kg, the methanol and aqueous extracts of *Andrographis lineata* significantly decreased blood glucose, T.C., LDL, and VLDL levels while increasing HDL levels in comparison to the control group, indicating their antidiabetic and antihyperlipidemic activity.[84]

4.2.5. *Annona squamosa* (Annonaceae)

When administered orally for 30 days to diabetic rats, the ethanolic extract of *Annona squamosa* leaves dramatically lowered the animals' blood glucose, glycosylated hemoglobin, urea, and

creatinine levels. The findings revealed that *Annona squamosa* had strong antidiabetic potential and that the effectiveness of the extract was equivalent to that of gliclazide.[85]

4.2.6. *Artocarpus heterophyllus* (Moraceae)

At a dosage level of 400 mg/kg p. o., the ethanol extract of *Artocarpus heterophyllus* dramatically lowered blood glucose levels in diabetic rats, demonstrating the plant's potent anti-hyperglycemic effect.[86]

4.2.7. *Asystasia gangetica* (Acanthaceae)

The ethanolic extract of *Asystasia gangetica* significantly reduced blood glucose, glycosylated hemoglobin (HbA1C), T.C., T.G., LDL, and VLDL levels in diabetic rats when administered orally for 28 days at dose levels of 100 and 200 mg/kg. The levels of catalase (CAT), superoxide dismutase (SOD), glutathione (GSH), glutathione reductase (G.R.), glutathione peroxidase (GPx), and glucose-6-phosphate dehydrogenase (G-6-PDH) are also increased, and lipid peroxidation is decreased. *Asystasia gangetica* demonstrated considerable antidiabetic and antioxidant action, according to the results.[87]

4.2.8. *Boerhaavia diffusa* (Nyctaginaceae)

In diabetic rats, the ethanolic root extract of *Boerhaavia diffusa* significantly decreased blood glucose, T.G., LDL, and T.C. levels but increased HDL and serum transaminase, such as serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), and serum alkaline phosphatase (SALP) activity, which indicated its anti-dia.[88]

4.3. Discussion

According to scientific studies, a number of plant species have the ability to effectively lower sugar levels. Numerous plant components, including phytoconstituents, were discovered to have strong antidiabetic action via the screening of antidiabetic medications. A summary of information on medicinal plants used to treat Diabetes has been provided in this review.

Africa	<i>Combretum micranthum, Ficus capensis, Cassia sieberiana, Ocimum sanctum, Anacardium occidentale, Jatropha curcas, Allium sativum, Citrus medica, Moringa oleifera, Catharanthus roseus, Tamarindus indica, Carica papaya, Landolphia dulcis, Mesonerum benthamianum, Ocimum viridae, Psidium guajava and Pterocarpus ericens</i>
Canada	<i>Abies balsamea, Acorus calamus, Aralia racemosa, Arisaema triphyllum, Celastrus scandens, Corylus cornuta, Gaultheria procumbens, Juniperus communis, Kalmia angustifolia, Nuphar variegatum, Picea mariana, Populus balsamifera, Populus tremuloides, Prunus serotina, Quercus alba, Quercus rubra, Sassafras albidum, Sorbus Americana, Taraxacum officinale, Thuja occidentalis and Verbascum thapsus</i>
China	<i>Astragalus membranaceus, Panax ginseng, Polygonatum odoratum, Lycium barbarum, Ophiopogon japonicus, Epimedium sagittatum, Lithospermum erythrorhizon, Rheum palmatum, Hordeum vulgare, Codonopsis pilosula, Momordica charantia, Punica granatum, Dioscorea opposita, Allium cepa, Trigonella foenum graecum, Prunella vulgaris and Ephedra sinica</i>
India	<i>Abroma augusta, Abutilum indicum, Aconitum palmatum, Asparagus racemosus, Berberis aristata, Catharanthus roseus, Costus speciosus, Ficus racemosa, Ipomoea batatas, Momordica charantia, Syzygium cuminii, Trigonella foenum graecum, Urtica dioica, Zingiber officinale, Allium cepa, Allium sativum, Aloe vera, Cajanus cajan, Gymnema sylvestre, Momordica charantia, Ocimum sanctum, Pterocarpus marsupium and Tinospora cordifolia.</i>
Bangladesh	<i>Abroma augusta L.f, Abutilon indium Sweet var, Acanthus ilicifolius L, Achyranthes aspera L, Adiantum capillus-veneris L, Allium sativum L, Alocasia macrorrhizos L. G. Don</i>

Table 01: Antidiabetic plants from different countries

Conclusion

Diabetes mellitus is a condition of fat, protein, and carbohydrate metabolism that is mostly brought on by decreased insulin secretion or the inhibitory effects of insulin. Natural remedies were utilized before there were synthetic pharmaceuticals, and they are being used today. Diabetes is a metabolic condition that has been linked to significant economic loss. In addition, poorly managed Diabetes causes a wide range of chronic consequences, including blindness, heart failure, and kidney failure. New hypoglycaemic and maybe antidiabetic medications need to be developed and researched in order to stop this worrisome health issue. This review examines herbal medicines that have shown significant hypoglycemic efficacy, sometimes even with considerable potency. Patients are increasingly asking to utilize natural medications with anti-diabetic properties. Around the globe, herbal medicine has been used effectively to treat a variety of diseases, including Diabetes.

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