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# Sustainable Pathways for Current and Future Preventions of Diabetes: A Critical Review

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**Abstract**

Diabetes mellitus, is characterized by elevated levels glucose in the body. To achieve good metabolic control in diabetes, a combination of pharmacological treatment and changes in the way of life is essential. There are various hypoglycemic agents such as herbal and synthetic drugs available for the treatment of diabetes. Herbal compounds are easily available, effective, have no side effects. In this comprehensive review article the reported hypoglycemic plants of India are helpful to the health professionals and scientists for developing alternative medicines to treat various types of diabetes. Treatment reduces the blood glucose level and other diabetic complications. Primary focus should be on changes in lifestyle. The aim of this article is to provide an update on the current and future benefits and restrictions of various drugs, for the treatment of diabetes.

***Keywords:*** Diabetes mellitus; Hypoglycemic agents; Herbal drugs; Synthetic drugs; Diabetic complications.

## 1. Introduction

Diabetes mellitus is a chronic disease, which need regular care and medicine. It is an endocrine metabolic disease. Diabetic patients suffer with the secretion of necessary amount of insulin for their bodies, which causes their blood glucose levels to rise (Kharroubi, 2015; Misra et al., 2011). More than 20 million people in India currently have diabetes, which puts our country at disaster level worldwide. By the year 2025, this number is expected to rise by almost fifty-seven million (Rai, 1995; Subash Babu et al., 2007). Figure. 1 shows various types of diabetes.

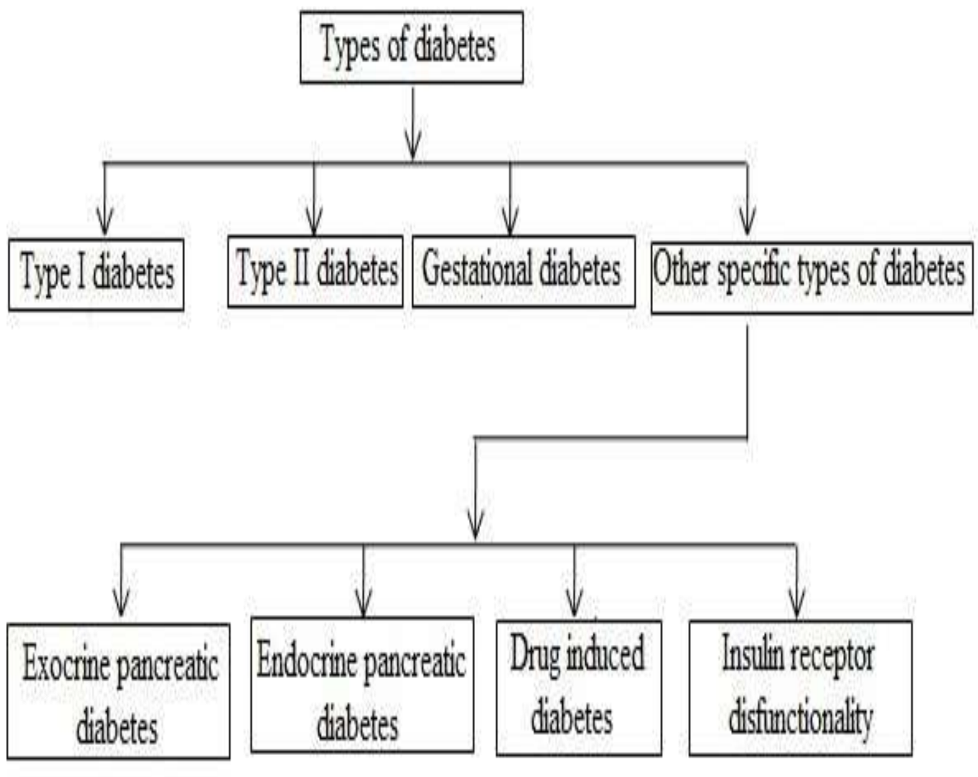


**Figure.1.** Various types of diabetes.

### *1.1 Type I diabetes*

This kind of diabetes, often referred to as insulin dependent diabetes mellitus (IDDM) or juvenile-onset diabetes (20 years of age or younger), it occurs due to the pancreatic beta cells inability to secrete insulin. Type I diabetes is brought on by disorders or injuries to the pancreatic beta cells that hinder the production of insulin (Bakhtiuary, 2011; Shukia et al., 2000). Heredity has been found significant factor in the death of beta cells. Beta-cells of diabetic patients are destroyed due to autoimmune diseases or viral infections. Rapid weight loss and ketonuria are signs of Type I diabetes (Awasthi et al., 2004; Srivastava et al., 2012).

### *1.2 Type II diabetes*

This type of diabetes is also known as adult-onset diabetes (over 30 years) or non-insulin dependent diabetes mellitus (NIDDM). It results from decreased insulin sensitivity of the target tissue. Compared to type I diabetes, type II diabetes is extra prevalent. Increased blood glucose levels, increased fat oxidation for energy, liver cholesterol production and decreased protein synthesis are symptoms of diabetes mellitus (Mahler and Adler, 1999; Oliveira et al., 2005). Type II diabetes symptoms and reducing weight are associated. The majority of body cells, with the exception of brain cells, are unable to utilize glucose because of lack of insulin. As a result, blood glucose concentration rises, cells utilize less glucose and consumption of protein and fat rises (Kooti et al., 2016; Rizvi and Mishra, 2013).

### *1.3 Gestational diabetes*

It is referred as hyperglycemia and typically detected for the duration of pregnancy. After delivery it can be disappeared. Diagnosis and management of gestational diabetes are essential as surplus maternal glucose crosses the placenta and causes excessive levels of fetal insulin production. It causes the risk of delivery trauma and can cause foetal macrosomia. Neonatal hypoglycemia may result in this case (Ahn et al., 2017; Chen et al., 2005; Chowdary and Aanandhi, 2018).

### *1.4 Other specific types of diabetes*

#### *1.4.1 Exocrine pancreatic diabetes*

Alcoholism, which damages the bulk of beta cells, is a prevalent cause of exocrine pancreatic illness. Cystic fibrosis, neoplasia, and chronic pancreatitis are few symptoms (Grover et al., 2002).

#### *1.4.2 Endocrine pancreatic diabetes*

It occurs as a result of excessive endogenous production of insulin-inhibiting hormones. Because of the endogenous release of glucagon and catecholamines, it can result in severe burns, acute myocardial infarction, and other health problems such aldosteronoma, phaeochromocytoma, acromegaly, cushing's syndrome, hyperthyroidism, stress hyperglycemia, and glucagonoma (District et al., 2017).

*1.4.3 Drug induced diabetes*

Some medications, such as corticosteroids, thiazide diuretics, phenytoin, nicotinic acid, pentamides, diazoxide, etc., can result in diabetes because they impair pancreatic beta-cell activity(Whiting et al., 2011).

*1.4.4 Insulin receptor dysfunctionality*

Both forms of quantitative and qualitative abnormalities in the insulin receptor are the cause of hyperglycemia (Bindu and Narendhirakannan, 2019).

## 2. Symptoms of diabetes

The two most prevalent kinds of diabetes are Type I and Type II. Patients with diabetes may have abrupt weight loss, extreme exhaustion, blurred vision, excessive thirst (polydipsia), frequent urination (polyuria) and other symptoms [20].

## 3. Diseases occur due to diabetes

*3.1 Cardiovascular disease*

Strokes and coronary heart disease brought on by obesity, hyperlipidemia, hypertension, smoking and hypercholesterolemia are risk factors for cardiovascular disease. Angina pectoris and congestive heart failure are two indications of cardiovascular problems (Serup et al., 2001).

*3.2 Diabetic ketoacidosis (DKA)*

The excessive production of ketone in the body results in insulin shortage, which leads to a metabolic acidosis. When insulin is absent, the body enters a catabolic condition when triglycerides are transformed into free fatty acids (Galicia-garcia et al., 2020).

*3.3 Diabetic micro angiopathy*

Blood vessels are affected due to diabetes mellitus. A structural abnormality in the blood vessel caused by an increase in membrane thickness can be sparked by diabetes, which subsequently progresses to a functional abnormality that decreases the blood vessels permeability to fluid and chemicals like albumin (Gohel et al., 2021; Wu et al., 2006). As a result, all blood vessels are harmed, which negatively impacts specific body organs like kidneys (causing diabetic nephropathy), the eyes (causing diabetes retinopathy and blindness due to visual symptoms) and the other organs (Shoaib, 2021).

## 4. Diagnosis of diabetes

*4.1 Physical examination*

A component of the minimal standards is a thorough examination of the human body. Measurements of height, weight, blood pressure, assessment of peripheral pulses, cardiovascular symptoms and ophthalmoscopy tests are some of the characteristics, utilized for the physical examination of the human body (Yang et al., 2019).

*4.2 Laboratory assessment*

A blood glucose measurement is a minimal condition for diagnosis confirmation. 80 mg/dl to 120 mg/dl of blood sugar is considered normal. These include the oral glucose tolerance test, fasting plasma glucose test, random plasma test, measurement of serum creatinine in all hypertensive patients, the examination of urine for protein, ketones and glucose, the electrocardiogram and the measurement of total serum cholesterol & triglycerides (Schloot et al., 2019).

**5. Treatment of diabetes**

The primary goal of the pharmaceutical industry is to provide safe, efficient and cost-effective drug supply to enhance the health of diabetic patients. The safe and appropriate use of drugs by people with diabetes is the pharmacist's responsibility (Das et al., 2023). An essential component of the proper management of diabetes is dietary counseling. The management of diabetes involves careful medication compliance, correct yoga practice and patient lifestyle adjustments (Gerber et al., 1998).There are several benefits of physical activities for diabetic patients. Studies in the literature advocate for regular physical activity programs for the treatment, prevention and education of diabetes problems. Diabetic patients are helped by ongoing educational programs and counseling to stress threat, and proper treatment along with change in lifestyle to avoid the recurrence of this deadly condition. Combination of non-pharmacological and pharmacological measures, such as altering lifestyle, diet, controlling body weight, physical activity, exercise and therapy of insulin can help to reduce the complications associated with diabetes. However, when these measures are insufficient to control diabetes, these herbal remedies and anti diabetic medications are used (Singh et al., 2023a).

*5.1 Various parameters used for prevention of diabetes*

The major components used for the cure of diabetes are:

- Dietary management
- Yoga and exercise
- Oral hypoglycemic medicine
- Therapy of insulin
- Herbal treatment

*5.1.1. Dietary management*

Healthy diet is essential in each case of illness. Drugs of diabetes mellitus can be helpful only while right awareness is given by health professionals to the patient.

*5.1.1.1. Aim of dietary treatment*

Fulfill the nutritional necessities, controlling of body weight, blood lipid level, blood glucose level and compatibility with various kinds of drugs like insulin and oral hypoglycemic medicines.

*5.1.1.2. Dietary guidelines for diabetic people*

Carbohydrates are good source of calories in the diet and it fulfills up to 60% requirement of the total calories. However, traditionally speaking, fiber-rich diet has been advised. The percentage of total calories that can be absorbed as fat in the diet should be kept to a maximum of 25 to 35%, but the percentage of total calories that can be consumed as saturated fat should not exceed 10%. The acceptable limit for cholesterol in meals is 300 mg per day and this amount should be maintained. Protein intake can range from 10 -15% of whole calories. Vegetables and animal should both be sources of protein. Salt overdose should be avoided. It may only be given to patients who have nephropathy or hypertension under specific conditions. Sorbital and fructose, are two nutritious sweeteners, and they should be used as moderated food (Richter et al., 2008).

Diabetic and non diabetic, both should take the same precautions while consuming alcohol. Alcohol may, however, increase the risk of hypoglycemia in patients using anti-diabetic medication. In a balanced diet, individual does not require the consumption of chemically produced vitamins and minerals, with the exception of pregnancy and lactation (Satpute et al., 2009).

*5.1.2. Yoga and exercise*

Type I and Type II diabetes, both need exercise therapy. Regular exercise has a number of advantages like regulating blood sugar level. It improved blood flow and facilitated the tissues to consume extra glucose. Figure. 2 shows various parameters used as preventive measures for diabetes.

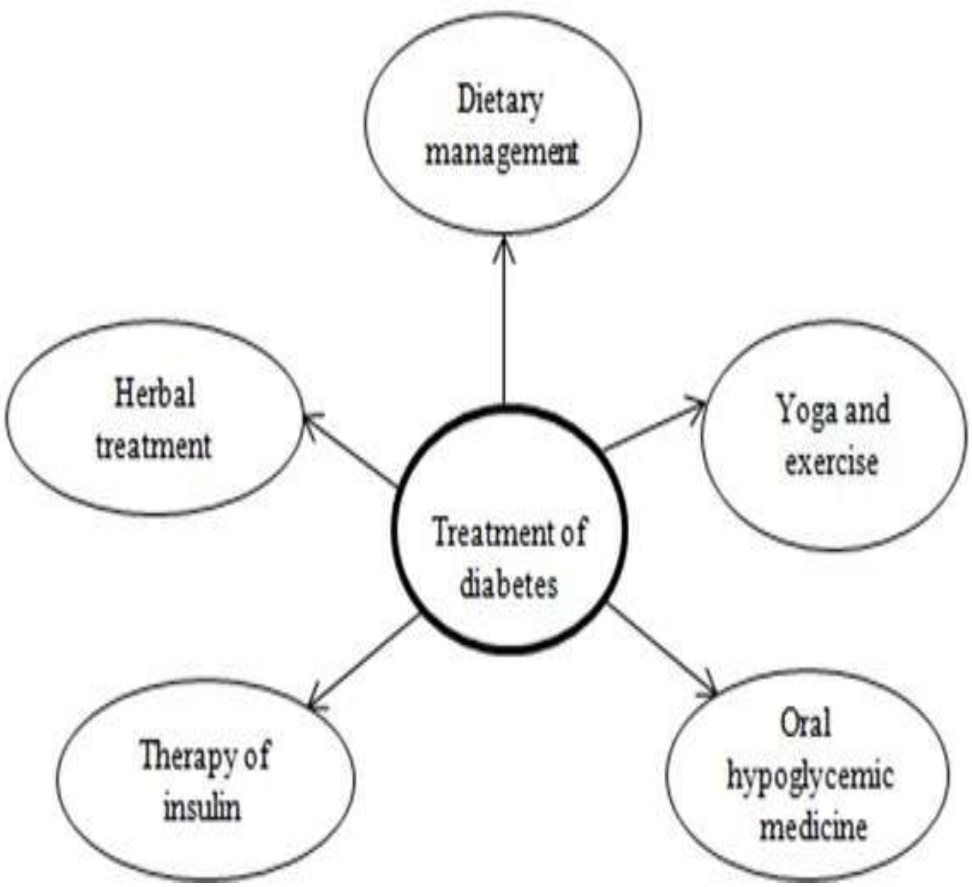


**Figure.2.** Parameters used for prevention of diabetes.

The human body benefits from physical activity by promoting weight loss and increasing the sensitivity of insulin, which decreases blood glucose level. Every person should follow a diet plan and practice yoga on a regular basis. Every person needs to adjust these programs for greater health and fitness. Yoga is a science that can have both healing and preventative implications for people with diabetes. It is a form of exercise that entails several asanas. Yoga helps to treat diabetes and enhancing mental health. Surya namaskar, padmasana, vajrasana, tadasana, bhastrika pranayama, kapalbhati, anulomviloma, and bhramari are some of the asanas that are useful for diabetes mellitus (Chiasson et al., 1994).

*5.1.3. Oral hypoglycemic medicine (OHM)*

When diet and exercise alone have not been enough to achieve the therapeutic goals, antidiabetic medications are used. Table 1 enlists several oral hypoglycaemic medicines along with their mode of action.

**Table 1.** Mode of action of some oral hypoglycaemic medicine.

| Oral hypoglycemic medicines | Mode of action |
|---|---|
| **Sulphonylureas** | |
| Chlorpropamide | |
| Glibenclamide | Secretion of insulin increased by beta cells of pancreas |
| Glimepiride | |
| Glipizied | |
| Glyburide | |
| Tolbutamide | |
| **Non Sulphonylureas** | |
| **A. Biguanides** | |
| Metformin<br>Phenformin | Metformin and phenformin diminishing the hepatic gluconeogenesis |
| **B. Meglitinides** | |
| Repaglinide<br>Nateglinide | Repaglinide and nateglinide inducing the beta cells for production of insulin |
| **Thiazolidinediones** | |
| Rosiglitazone<br>Pioglitazone | Thiazolidinediones increase insulin sensitivity in skeletal muscle and dipose tissues |
| Miglitol | **Alpha - Glucosidase inhibitors** |
| Acarbose | |

| | |
|---|---|
| Alpha- Glucosidase inhibitors | increase absorption of glucose by inhibiting the alpha - Glucosidase enzyme |

*5.1.3.1 Sulphonylureas*

Sulphonylureas work by inducing the pancreatic beta cells to release of insulin and by enhancing its effects via extra pancreatic pathways. If the pancreatic beta-cells are unable to release the sufficient quantity of insulin for the patient, sulphonylureas are ineffective. There are several sulphonylureas in the market, but choosing the right one will depend on a number of criteria, including availability, cost, side effects and doctor's experience. Because of their negative side effects and prolonged duration of action, the first generation sulphonylureas including glibenclamide, tolbutamide, and chlorpropamide are frequently avoided. Sulphonylureas of the second and third generations, including glimepiride, glipizide and glyburide are often utilized (Kolak et al., 2007). Sulphonylureas have been linked to hypoglycemia, hence it is important to monitor their use in the elderly population.

Tolbutamide is a sulphonylurea with a relatively short half-life that may be favored in diabetes to individuals who had renal decline.

*5.1.3.2 Biguanides*

Biguanides work by reducing gluconeogenesis (production of hepatic glucose) and boosting the utilization of glucose in peripheral tissues. The liver typically releases glucose after determining the blood insulin level. When blood insulin level are high, the liver generates little glucose. The liver generates more glucose when the blood level of insulin is lower. Metformin lowers glucose synthesis by sensitizing the liver to insulin circulation. Metformin is typically used in overweight diabetic patients when nutritional therapy does not work. It is contraindicated in patients over the age of 70 with impaired renal function, patients with different disorders such heart failure, hepatic injury and propensity to lactic acidosis due to the activity of lactic acidosis. In such a situation, metformin should not be used to treat any kind of infections, concurrent diseases or surgical procedures. Biguanides and sulphonylureas are to be avoided during pregnancy and breast feeding. There are several drugs made from conventional herbs that can be used to lower blood glucose level, but their long-term effectiveness and safety are found low. Therefore, the medical community does not advise this course of treatment (Kolak et al., 2007).

*5.1.3.3 Meglitinides*

Meglitinides work by encouraging the pancreatic beta cells of the langerhans to release insulin, hence lowering blood glucose levels. Meglitinides have a shorter duration of action than sulphonylureas, despite the greater effectiveness. They need to be taken three times daily because of their brief duration of effect. Repaglinide and nateglinide are two types of meglitinides (Machry et al., 2018).

*5.1.3.4 α- Glucosidase inhibitors*

α-Glucosidase inhibitors work by preventing the enzyme glucosidase from absorbing glucose. Acarbose and miglitol are two examples of α- Glucosidase inhibitors. By delaying the digestion and absorption of carbohydrates in the colon, they lower blood glucose level.

*5.1.3.5 Thiazolidinediones*

Thiazolidinediones promoted insulin sensitivity, which decreases hepatic glycogen synthesis (glucogenesis) and increases absorption of muscle glucose that is insulin dependent. In adipose tissues and skeletal muscle, thiazolidinediones, sometimes referred to as glitazones, enhance insulin sensitivity like Rosiglitazone and Pioglitazone (Machry et al., 2018).

*5.1.4. Therapy of insulin*

Insulin treatment is necessary in order to achieve optimal metabolic control by mimicking physiological insulin and reducing the risk of hypoglycemia.

*5.1.4.1. Types of insulin preparations*

There are two different types of insulin preparations are as follows:

- Intermediate acting
- Short acting

*5.1.4.1.1 Intermediate acting*

Multiple dosage insulin treatment may be utilized if the optimal dose of combination therapy is insufficient to achieve the aim. Long acting insulin is not often required, with a few rare exceptions. The crucial component of care is insulin therapy, which cannot be adequately addressed without adequate patient understanding. As a member of the healthcare team, patients and their families must work together effectively.

*5.1.4.1.2 Short acting*

During treatment of Type II diabetes, insulin is often recommended, especially in the situations of pregnancy, breast feeding, acute sickness, surgery, stress, hyperglycemia and severe metabolic breakdown including diabetic ketoacidosis and lactic acidosis.

*5.1.4.2 Insulin regimens*

Insulin doses are administered subcutaneously. In situations of diabetic ketoacidosis, additional methods such as intravenous or intramuscular, may also be employed. Other methods such as intraperitoneal and nasal are now in the experimental stage. The patients will require one or more injections daily for excellent glycemic control. However, doctors may advise patients to have daily injection of an intermediate acting medication. Typically, two times per day, a combination of short-acting and intermediate acting insulin may be utilized. Patients may receive a combination of both types (intermediate acting and short) of insulin dosage in the morning while dealing with connected diabetes concerns. Then, short-acting insulin doses are administered to these patients before lunch and dinner, an evening dosage of intermediate-acting insulin is recommended to the patients in the night. On the basis of the same principles, different medical treatments may be selected. Another option is to adopt a treatment course that combines many short-acting insulin injections prior to meals with proper amount of intermediate-acting insulin before bedtime in cases of rigorous glycemic control (Thordardottir et al., 2019).

*5.1.4.3. Techniques of insulin delivery*

Plastic disposable syringes with a fixed needle are often utilized. Plastic syringes can be reused if safety precautions are required to avoid contamination. In actual fact, there should be no use of alcohol or antiseptic chemicals for needle wiping or syringe cleansing. Due to lack of plastic syringes, properly disinfected glass syringes may be used instead. Injections should be made into the deep subcutaneous tissue at an angle of 90° or 45°. Rotating the injection sites is another suggestion for preventing harm to the insulin injection sites. Other insulin administration methods include insulin injection pens, which are generally secure and simple to use. Although the cost of a pump therapy is higher than that of other options, it offers continuous subcutaneous insulin delivery. This might lead to issues, thus it calls for expertise and efficient maintenance facilities. In comparison to the thighs or upper arms, the abdominal region absorbs insulin more quickly. Therefore, it may be selected for quick-acting medicines. The awareness of patient and fundamental abilities needed for administration should be frequently assessed while on insulin therapy (Singh et al., 2023b).

*5.1.5 Herbal treatment for diabetes mellitus*

Numerous plant species have been shown in the literature to have anti-diabetic properties. Although the pharmaceutical industry has generated several anti-diabetic medications, diabetes and the consequences it causes are still serious health issues. A number of medicinal plants have recently been shown to be effective in the treatment of diabetes and used as diabetic and hyperlipidemic medications. Numerous medicinal plants have been utilized as anti-diabetic medications in the Ayurvedic medical system as described in old Indian texts including the Sushrut Samhita, Charak Samhita, and Astang Hriday (Singh et al., 2023b).

Diabetes is spreading quickly over the entire world and in every region of our country. Research on natural compounds with anti-diabetic effects is therefore in high demand (Singh et al., 2023c). Several plant species have been shown to be quite beneficial for treating diabetes in India such as *Ficus bengalensis* (Moraceae), *Coccinia indica* (Cucurbitaceae), *Syzygium cumini* (Myrtaceae), *Tinospora cordifolia* (Menispermaceae), *Andrographis paniculata* (Acanthaceae), *Trigonella foenum graecum* (Papilionaceae), *Gymnema sylvestre* (Asclepiadaceae), *Morus nigra*(Moraceae), *Citrus aurantum* (Rutaceae), *Eugenia jambolana* (Myrtaceae), *Azadirachta indica* (Meliaceae), *Pterocarpus marsupium* (Fabaceae) and *Momordica charantia* (Cucurbitaceae) (Nasri et al., 2014; Singh et al., 2022).

A variety of medicinal herbs, commonly used for more than 1000 years and known as Rasayana, are found in herbal formulations used in traditional Indian healthcare systems. Several medicinal plants have been studied due to their potential to treat diabetes (Kavishankar et al., 2011; Singh et al., 2021). We must create new formulas and technologies that will enable us to generate inexpensive, efficient herbal medicines with minimal side effects. Plants have been utilized as medicine from the dawn of time to cure diabetes as well as other illnesses. Alkaloids, glycosides, phenols, terpenoids, flavonoids, tannins, resins, saponins, polysaccharides and amino acids are a few phyto-chemicals that are the key active constituents that produce antidiabetic action with various mechanisms (Abd El-Mawla et al., 2011).

*5.1.5.1 Mechanism of action of herbal antidiabetics*

Different mechanisms underlie the antidiabetic effects of herbs. The following are possible categories for how anti-diabetic plant mechanisms of action work (Jarald et al., 2008).

- Insulin secretion stimulation
- Lowering of insulin resistance
- Reabsorbing renal glucose is inhibited
- Induction of hepatic glycolysis and glycogenogenesis
- Galactocidase and glucocidase inhibition
- Pancreatic -cell regeneration and repair
- Preventing the abnormal conversion of glucose from starch
- Protection against the -cells' annihilation
- Activities that reduce cortisol and inhibit alpha-amylase
- The islets of Langerhans' cell size and density increasing
- An improvement in digestion, as well as a decrease in urea and blood sugar
- Adrenomimeticism, potassium channel blockade in pancreatic beta-cells, and CAMP activation
- Inhibition of insulin deteriorative processes and stimulation of insulin production from islet -cells.
- Giving the beta -cells access to certain essential elements including magnesium, calcium, zinc, copper, and manganese.

*5.1.5. 2. Indian medicinal plants with anti diabetic activity*

Since ancient times (2500 BC), diabetes has been acknowledged in Ayurveda, and its treatment has been recommended. Many scientists have conducted extensive research on the majority of the plants used in Ayurveda to treat diabetes. For the treatment of diabetes, there are several new plant medications available as listed in Table 2.

**Table 2.** Indian medicinal plants with antidiabetic activity.

| **Plants name** | **Parts of plant used** | **Mode of action** | **References** |
|---|---|---|---|
| *Allium sativum* (Garlic) | ***Bulb***  | Improved the insulin release from beta-cells of pancreas | (Eidi et al., 2006) |
| *Abrus precatorius* (Ratti) | ***Leaves***  | Controlling the carbohydrate metabolizing enzyme to maintains the glucose homeostasis | (Patel et al., 2012) |
| *Wattakaka volubilis* (Perun-kurinjan) | ***Leaves***  | glucose and lipids level decrease in serum | (Ayyanar et al., 2008) |
| *Ficus bengalensis* (Banyan tree) | ***Barks***  | Increase the insulin secretion and blood glucose response | (Ayyanar et al., 2008) |

| | | | |
|---|---|---|---|
| *Ocimum sanctum* (Tulsi) | ***Leaves***  | Decline glucose level in the blood | (Prakash and Gupta, 2005) |
| *Azadirachta indica* (Neem) |  | Improve the conversion of glucose to glycogen | (Rajesham et al., 2012) |
| *Trigonella foenumgraecum* (Fenugreek) | ***Seeds***  | Improve the glucose stimulated insulin release from islet cells | (Modak et al., 2007) |
| *Cinnamomum zeylanicum*(Cinnamon) | ***Leaves and barks***  | Beta-cells of pancreas are regenerated and repaired | (Subash Babu et al., 2007) |
| *Ficus carica* (Anjir) | ***Leaves and fruits***  | prevention of MMPs can recover oxidative stress and insulin resistance | (Serraclara et al., 1998) |

| | | | |
|---|---|---|---|
| *Aloe vera* (Ghritkumary) | ***Leaves***  | Stimulates the beta-cells of pancreas for production and release of insulin | (Tanaka et al., 2006) |
| *Momordica charantia* (Bitter gourd) | ***Fruits***  | Prevent the fructose-1, 6-biphosphatase as well glucose-6-phosphatase in the liver | (John A.O. Ojewole, 2005) |
| *Mangifera indica* (Mango) | ***Leaves***  | Decrease the absorption of glucose in intestinal | (John A.O. Ojewole, 2005) |
| *Glycine max* (Soya beans) | ***Seeds***  | Diminish the glucose level in plasma | (Kang et al., 2006) |
| *Morus alba* (Mulberry) | ***Leaves and fruits***  | Alpha-glycosidase enzyme inhibitor action | (Kwon et al., 2011) |

| | | | |
|---|---|---|---|
| *Murraya koenigii* (Curry-leaf) | ***Leaves and Fruits***  | Normalized the actions of liver glucose 6-phosphatase, hexokinase and HMG Co A reductase enzymes | (Adebajo et al., 2006) |
| *Tinospora cordifolia* (Guduchi) | ***Stem***  | Decline the level of glucose in urine and blood | (Adebajo et al., 2006) |
| *Tamarindus indica* (Tamarind) | ***Seeds and Fruits***  | Controlling the level of glucose in blood | (Fröde and Medeiros, 2008) |
| *Cajanus cajan* (Pigeon pea) | Seeds and leaves  | Diminish the level of glucose in plasma | (Matsushita et al., 2019) |
| *Cassia auriculata* (Tanner's cassia) | ***Flowers***  | Prevent the re absorption of renal glucose | (Hatapakki et al., 2005) |

| | | | |
|---|---|---|---|
| *Acacia arabica* (Babul) | ***Seeds and barks***  | Induced the hypoglycemic action through release of insulin from beta-cells of pancreas | (Arowosegbe et al., 2015) |
| *Artocarpus heterophyllus* (Jackfruit) | ***Fruit***  | Inhibit absorption of glucose from gut | (Ayodhya et al., 2010) |
| *Eucalyptus globules* (Blue gum) | ***Leaves***  | Enhance secretion of insulin from clonal pancreatic β-line | (Chauhan and Rathod, 2020) |
| *Withania somnifera* (Winter cherry) | ***Leaves***  | Raise regeneration and stimulation of beta-cells of pancreas | (Malviya et al., 2010) |
| *Allium cepa* (Onion) | ***Bulb***  | Prohibited lipids and glucose in blood serum | (El-Demerdash et al., 2005) |

| | | | |
|---|---|---|---|
| *Xanthocercis zambesiaca* (Nyala tree) | ***Leaves***  | Decrease in resistance of insulin | (Nojima et al., 1998) |
| *Lyciumbar barum* (Chirchita) | Fruits  | Improved the insulin like action of plasma | (Nojima et al., 1998) |
| *Aegle marmelos* (Golden apple) | Leaves, seeds and fruits  | Stimulates the glucose-6-phosphate dehydrogenase enzymeactions of liver | (Kesari et al., 2006) |
| *Brassica juncea* (Mustard) | Seeds and leaves  | Suppressed the action of gluconeogenic and glycogen phosphorylase enzymes | (Yokozawa et al., 2002) |
| *Beta vulgaris* (Beetroot ) | ***Whole plant***  | Raise the hepatic glycogen concentration and decrease level of glucose in blood | (Chan et al., 2012) |

| | | | |
|---|---|---|---|
| *Capsicum frutescens* (Chilli) | ***Fruits***  | Enhance level of insulin in plasma and improves tolerance of glucose | (Tolan et al., 2004) |
| *Coriandrum sativum* (Coriander) | ***Leaves***  | Decline level of glucose in blood by decreasing in gluconeogenesis and glycogenolysis | (Gray and Flatt, 1999) |
| *Catharanthus roseus* (Red periwinkle) | ***Whole plant***  | Raise glycogenesis and metabolism of glucose | (Khedkar et al., 2010) |
| *Curcuma longa* (Turmeric) | ***Rhizome***  | Decrease level of glucose in blood by regeneration of beta - cells | (Honda et al., 2006) |
| *Zingiber officinale* (Ginger) | ***Rhizome***  | Reduce level of glucose in blood by preventing re absorption of glucose | (Kato et al., 2006) |

| | | | |
|---|---|---|---|
| *Cuminum cyminum* (Cumin seed) | ***Seeds***  | Maintain glucose homeostasis through controlling carbohydrate metabolizing enzymes | (Bnouham et al., 2006) |
| *Psidium guajava* (Guava) | ***Leaves and Fruits***  | Enhance insulin discharge from beta cells of pancreas | (J. A.O. Ojewole, 2005) |
| *Gymnema sylvestre* (Gurmar) | ***Leaves***  | Decrease level of glucose in plasma by increasing the utilization of peripheral glucose | (Sugihara et al., 2000) |
| *Triticum vulgare*(Wheat) | ***Whole plant***  | Enhance glucose use by increased glycolysis | (Kodama et al., 2005) |
| *Hordeum vulgare* (Barley) | ***Seeds***  | Decline synthesis of glucose by decreasing of gluconeogenic enzyme | (Poppitt et al., 2007) |

| | | | |
|---|---|---|---|
| *Nelumbo nucifera* (Sacred lotus) | ***Flower***  | Improve oxidation of glucose via activation of enzyme glucose-6-phasphate dehydrogenase | (Huralikuppi et al., 1991) |
| *Coccinia indica* (Ivy-gourd) | ***Fruits***  | Reduce in level of glucose in blood through rising the action of liver hexokinase enzyme, resulting in efficient hypoglycemic action | (Ravi Kumar et al., 2011) |
| *Moringa oleifera* (Moringa) | ***Whole plant***  | It exhibits improved glucose tolerance and normoglycemia | (Bever and Zahnd, 1979) |
| *Amaranthus Esculentus* (Amaranth) | ***Whole plant***  | Prevent degradative processes of insulin | (Kim et al., 2006) |
| *Terminalia chebula* (Chebulicmyrobalan) | ***Seeds and fruits***  | Inhibitors of α-glucosidase enzyme | (Rao and Nammi, 2006) |

| | | | |
|---|---|---|---|
| *Piper betle* (Pan) | ***Leaves***  | Raise glucose utilization by uptake of glucose stimulation | (Santhakumari et al., 2006) |
| *Punica granatum* (Pomegranate) | ***Fruits***  | Take action via rising the glucose uptake | (Balducci et al., 2014) |
| *Carica papaya* (Papaya) | ***Fruits***  | Reduce gluconeogenesis and glycogenolysis and enhancing glycogenesis | (Makheswari and Sudarsanam, 2012) |
| *Syzygium cumini* (Jamun) | ***Seeds***  | Enhance glucose utilization and induced secretion of insulin by beta-cells of pancreas | (Oliveira et al., 2005) |
| *Panax ginseng* (Ginseng) | ***Fruits***  | Inhibits α-glucosidase enzyme and diminish level of glucose in blood | (Modak et al., 2007) |

## 6. Treatment of diabetes in future

All anti-diabetic medications have side effects and are costly, therefore finding innovative anti-diabetic regimens with fewer side effects and lower costs is a difficult task for researchers.

### *6.1. Polyphenols*

By enhancing cellular glucose absorption and regulating glucose metabolism through a variety of metabolic pathways, natural products with high polyphenol content can reduce insulin resistance (Solayman et al., 2016).

### *6.2. Smart insulin patches*

A narrow square containing an insulin patch has more than 100 tiny needles. The biocompatible patch technology is quick and simple to use. The patches are made of very small, painless needles that are packed with glucose and insulin-sensitive enzymes in tiny storage compartments. When the blood glucose level rises, the patches release these enzymes. The patch decreased blood glucose in a rat model for up to 9 hours. There is a possibility that the patch will work longer on diabetic people (Yu et al., 2015).

### *6.3. Microspheres*

Microspheres, also known as microparticles, are comprised of freely moving powders. They are fewer than 200 micrometers in size and have a significant surface area. The protective components that make up biodegradable micro particles include natural waxes, polymers and modified natural goods including starch, proteins, gums and lipids. Microspheres are valuable tools for topical, nasal, parenteral and oral roots. Microspheres could be appropriate for the creation of an oral version of insulin (Wong et al., 2018).

### *6.4. Oral insulin*

An innovative method of treating Type-II diabetes mellitus patients is by giving them insulin orally. Insulin administered orally has a stronger physiological impact than insulin administered parenterally. Compared to parenteral delivery of insulin, its initial pass through the liver lowers the risk of hypoglycemia, glycogenolysis and hepatic glucose generation. These points suggesting that could be a novel approach to the treatment of diabetic patients (Khedkar et al., 2010).

### *6.5. Dendrimers*

Dendrimers are artificial polymeric nanoparticles with a structure like a tree and are very branching. Dendrimers have a diameter of 2 to 10 nm. Polyamidoamine dendrimers are often utilized. Animals treated with polyamidoamine have lower blood glucose level than untreated animals. Dendrimers have been proposed as a potential therapy option for diabetic individuals (Rezaei-kelishadi et al., 2014).

**7. Conclusions**

The primary goal of the pharmaceutical industry is to provide safe, efficient and cost-effective drug to enhance the health of diabetic patients. The management of diabetes involves careful medication, correct yoga practice and patient lifestyle. Many scientists have conducted extensive research on the majority of the plants used in Ayurveda to treat diabetes. Diabetes is a very common endocrine disorder, affecting millions of people in the world. A collection of metabolic illnesses such as this one is characterized by hyperglycemia occurs due to deficiencies in insulin production, action or both. The limited number of commercially accessible diabetic medications still present, the rise in resistance and populations of patients who may be at risk all contribute to a variety of side effects and other issues, including undesired hypoglycemia impact. These factors have made it more appealing to focus research on historically accessible medicines that have few adverse effects, a wide spectrum of bioactivity and do not require laborious pharmaceutical manufacture. Therefore this review seeks to serve invoke more interest in bio screening of many medicinal plants as possible for their hypoglycemic potential. Such efforts will aid development of plant-derived novel anti hyper glycemic agents.

**List of abbreviations**

IDDM = Insulin Dependent Diabetes Mellitus

NIDDM = Non- Insulin Dependent Diabetes Mellitus

DKA = Diabetic Ketoacidosis

OHM = Oral Hypoglycaemic Medicine

**Statements and Declarations**

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**Authors contribution**

Sunita Singh: Writing - original draft, Mukul Sengar: Formal analysis, Vinay Mishra: Writing – reviewing and editing, Deepak Singh & Suresh Kumar Patel: Writing – reviewing and editing, Visualization, Anshuman Mishra: Data curation, Balendu Shekher Giri: Editing, Validation, Dhananjay Singh: Conceptualization, Investigation, Resources, Supervision.

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