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OVERVIEW ON DIABETES MELLITUS AND HERBAL DRUGS

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ABSTRACT

Diabetes mellitus (DM) is a metabolic condition defined by hyperglycaemia caused by pancreatic islet insulin secretion deficiency. It occurs more frequently worldwide. The condition is characterized by hyperglycaemia, with target cells displaying reduced responsiveness to insulin. Type II diabetes mellitus has 80 % to 90% of all cases of diabetes mellitus. This review aims to raise awareness of Diabetes mellitus, examining its types, symptoms, treatment, diagnosis, epidemiology and dietary considerations. Additionally, this article overviewed Herbs used for treatment of diabetes in detail. A variety of plant-derived active compounds representing numerous phytochemicals have consistently demonstrated hypoglycemic activity, implying their potential utility in the treatment of diabetes mellitus. Here example of some herbs which have Anti Diabetic properties are given.

KEYWORDS:- Diabetes Mellitus, Treatment, Complications, Herbs, Herbal Tablet.

INTRODUCTION

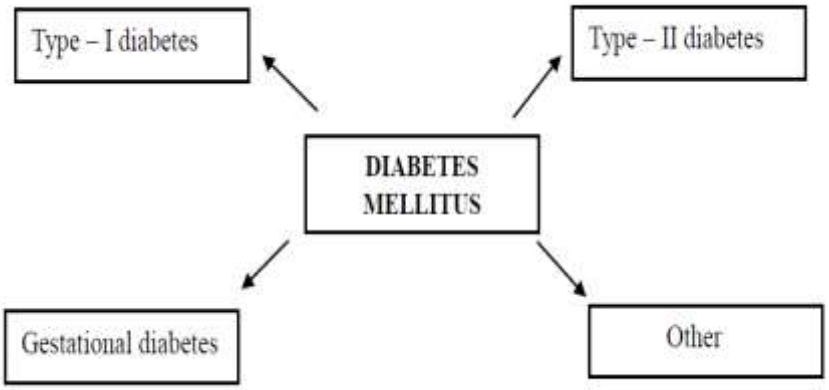
The word “Diabetes” & “Mellitus” were originated from Greek and Latin language. Where the word "Diabetes" means "to pass through" and "mellitus" means "sweet."

“As per WHO, Diabetes Mellitus is defined as heterogenous metabolic disorder characterized by common feature of chronic hyperglycaemia with disturbance of carbohydrate, protein and fat metabolism”.

Diabetes mellitus is a type of insulin resistance syndrome distinguished by a persistently high blood sugar level. Ancient Egyptians 3000 years ago explained this. This disease is commonly known as diabetes/ sugar disease. Diabetes mellitus is a noncommunicable disease.[1] Long-term consequences include cardiovascular disease, stroke, chronic nephropathy, and foot ulcers, among others. "Diabetes Insipidus", which is kidney related fluid retention problems are caused.

Type II diabetes mellitus has 80 % to 90% of all cases of diabetes mellitus. Moreover, people having diabetes mellitus who does the excess amounts of physical activity have lower risk of death than inactive persons. It is now well documented that some genetic constitutions are required for this event, which causes the growing burden of diabetes and other noncommunicable diseases, which is one of the biggest health issues for economic development plaguing the world's population.[2,3]

Classification of diabetes mellitus



1. Type 1 diabetes

Insulin-dependent diabetes mellitus occurs when the pancreas fails to produce insulin, which is required for survival. This type is most common in children and adolescents, but it is becoming more common later in life.

2. Type 2 diabetes

Non-insulin-dependent diabetes mellitus causes the body to respond incorrectly to the action of insulin produced by the pancreas. It is a much more common type of diabetes, accounting for approximately 90% of all diabetes cases worldwide. It mostly affects adults, but it is becoming more common in adolescents as well.

3. Gestational diabetes

It is the type of diabetes caused by pregnancy, known as gestational diabetes. To some extent, pregnancy causes insulin resistance. It is discovered in the middle or late stages of pregnancy. Because high blood sugar levels in a mother are transmitted to the baby via the placenta, gestational diabetes must be managed to protect the baby's growth and development. Gestational diabetes affects between 2% and 10% of all pregnancies.

4. Diabetes caused by other factors

It is caused by genetic defects or long-term use of unsafe medications.[4,5]

Symptoms

1. Type 1 diabetes

Type 1 diabetes is characterized by excessive craving, excessive thirst, unintentional weight loss, frequent micturition, hazy vision, sluggishness, and mood swings.

2. Type 2 diabetes

Excessive craving, thirst, frequent micturition, foggy vision, sleepiness, bruises that take a long time to heal, and recurrent contaminations.

5. Gestational diabetes

Gestational diabetes is frequently detected during a standard glucose test or an oral glucose resilience test, despite the fact that the majority of women do not experience symptoms. A woman with gestational diabetes may also experience excessive thirst or frequent micturition in rare cases.

General indications

Increased yearning, increased thirst, weight loss, frequent micturition, foggy vision, and injuries that will not heal.

Manifestations in men- Regardless of the general signs of diabetes mellitus, men with diabetes may experience decreased sex drive, Erectile dysfunction (ED), and poor muscle quality.

Manifestations in women- Symptoms in Women- Diabetes can cause a variety of symptoms in women, including urinary tract infections, yeast infections, and dry, itchy skin.[5]

Epidemiology of diabetes mellitus

Diabetics are becoming more common everywhere. Diabetes affected an estimated 285 million people worldwide in 2010, with type II diabetes accounting for roughly 90% of cases. According to the International Diabetes Federation, 381 million people had diabetes in 2013, and the number is rapidly increasing. According to the IDF Diabetes Atlas (2021), approximately 10% of the adult population aged 20-79 years has diabetes, with half of them being unaware that they have the disease. Diabetes affects more than 250 million people worldwide, with the number expected to rise to 350 million by 2030.[6,7]

Pathophysiology

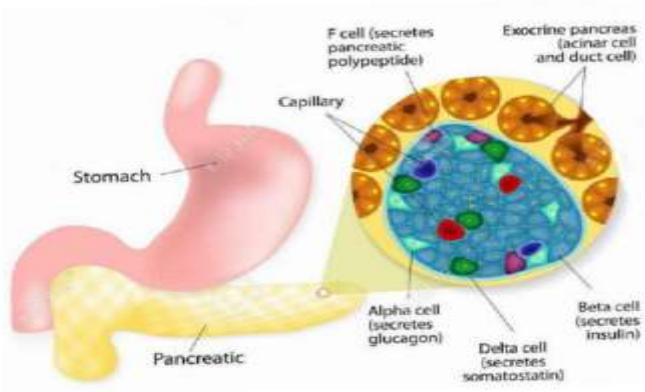


Figure 1: Stomach and pancreas in insulin formation.

Hormones are crucial in the regulation of the body's metabolic activities, particularly in the maintenance of blood glucose homeostasis.

The pancreas serves as both an endocrine and exocrine gland. In its endocrine function, it produces the peptide hormones insulin, glucagon, and somatostatin, while as an exocrine gland, it generates digestive enzymes. These peptide hormones are secreted by cells located in the islets of Langerhans.

Specifically

- Beta (B) cells produce insulin.
- Alpha cells produce glucagon.
- Delta (δ) cells produce somatostatin.

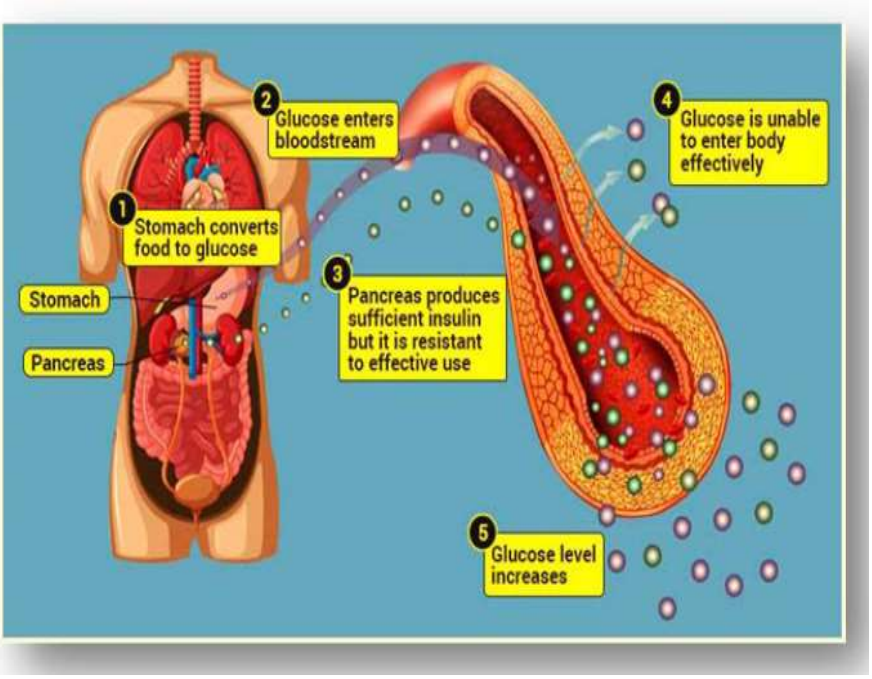


Figure 2: Pathophysiology of diabetes mellitus.

Insulin

Insulin was discovered in 1921 by Banting and best who demonstrated the hypoglycaemic action of an extract of pancreas. In 1922 an extract containing insulin was first used on a 14-year-old boy suffering from severe diabetes mellitus with excellent response. Insulin was then purified in a few years.

Type I diabetes: This is a chronic autoimmune disorder that causes the destruction of insulin-producing cells. Type 1 diabetics typically develop symptoms during adolescence and are not obese when they do so.

Type II diabetes mellitus: Type II diabetes mellitus is caused by insulin resistance, which reduces insulin production due to pancreatic beta cell failure. This causes a decrease in glucose transport into the liver, muscle cells, and fat cells. Insulin resistance and impaired insulin secretion are the root causes of type II diabetes. These patients are frequently obese and are usually seen in adults. Insulin resistance causes plaque formation and hyperphosphorylation. In contrast, an inactive lifestyle is a significant risk factor for type II diabetes mellitus. Exercise is therefore critical in patients.[7,11]

Complications associated with diabetes mellitus

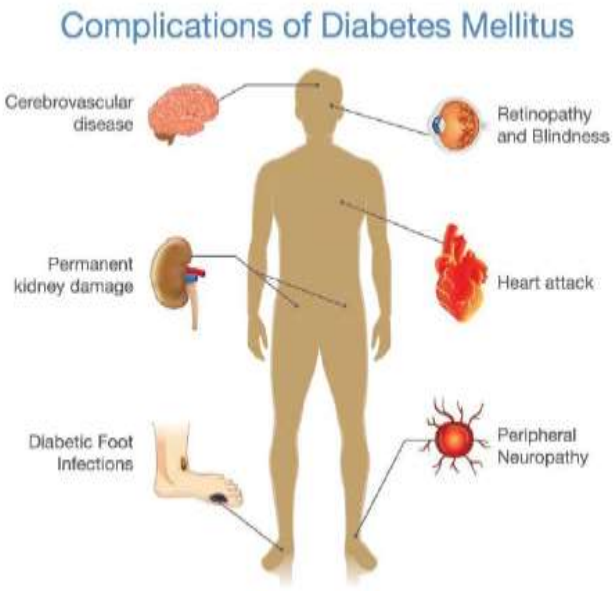


Figure 3: Complications of diabetes mellitus.

- Diabetic retinopathy is a major cause of blindness and visual impairment. Diabetes mellitus is associated with damage to the small blood vessels in the retina, which results in vision loss.
- Diabetes is one of the primary causes of kidney failure, though its prevalence varies by population and is also related to the severity and duration of the condition.
- In industrialized countries, heart disease is responsible for about 50% of all deaths in individuals with diabetes.[8]
- Diabetic neuropathy, or nerve damage caused by diabetes, can occur when too much sugar damages the walls of the tiny blood vessels (capillaries) that supply the nerves, especially in the legs.
- Foot damage increases the risk of various foot complications due to nerve damage in the feet or insufficient blood flow to the feet
- Skin and oral conditions - Diabetes can make you more prone to skin problems such as bacterial and fungal infections.
- Hearing impairment - Diabetes patients are more likely to have hearing problems.
- Alzheimer's disease - Diabetes type 2 may increase the risk of dementia, such as Alzheimer's disease.[9]

Treatment

Diet and physical activity are the primary approaches to non-pharmacological diabetes treatment. Approximately 40% of diabetics rely on oral agents to maintain adequate blood glucose control, while the remaining 40% require insulin injections10. Insulin, discovered by Banting and Charles Best in Canada in 1921, revolutionized diabetes treatment, transforming type 1 diabetes from a fatal disease to one with a chance of long-term survival. People with type 1 diabetes typically rely entirely on insulin injections for survival, which must be administered daily11. The majority of diabetes cases are type 2, and while not all of them require insulin for survival, roughly one-third of these people require insulin to manage their blood glucose levels.

A) Dietary Management and Physical activity

Changing eating habits and increasing physical activity are usually the first steps in lowering blood sugar levels. Our teaching centre organizes workshops to provide patients with valuable information about food nutrient content, healthy cooking practices, and exercise.[12]

Example- Broccoli, tomatoes, berry, apple, fish, etc.

B) Insulin therapy

Individuals with type 1 diabetes frequently require multiple daily insulin injections to maintain safe insulin levels. Diabetes type 2 frequently necessitates the use of insulin as a treatment. An insulin pump is an alternative to insulin injections. This pump, which is about the size of a pager, is usually worn on your belt. It delivers insulin via a small tube (catheter) inserted beneath the skin, usually in the abdomen.

C) Oral medications

Even when individuals with type 2 diabetes maintain a healthy diet and exercise regimen, there are instances when their blood sugar levels remain elevated. In such cases, healthcare providers may prescribe medications in pill form. These medications work by enhancing the body's natural insulin, decreasing blood sugar production, increasing insulin production, and inhibiting blood sugar absorption. Diabetes medications taken orally are occasionally used in conjunction with insulin.[12,13]

Examples of such medications include Metformin and Glimepiride.

D) Pancreas transplant

Diabetes is primarily treated by administering insulin to compensate for what the pancreas cannot produce. Patients can potentially avoid or delay the development of various diabetes-related complications by vigilantly monitoring their blood sugar levels to determine the appropriate insulin dosage.[14]

In cases where standard treatments prove ineffective, pancreas transplantation may become a viable alternative. A successful pancreas transplant can benefit patients by restoring insulin production, allowing them to

- Manage type 1 diabetes kidney complications
- Eliminate the need for insulin injections
- Reduce or eliminate dietary and physical activity limitations.
- Reduce or eliminate the risk of severe hypoglycemia.

Diabetes-related depression is a common problem, with symptoms appearing in both type 1 and type 2 diabetics. Untreated gestational diabetes can cause foetal death before or soon after birth.[15,16]

Herbal medicine

Herbal medicine has become the remedy for most of the diseases. In conjunction with a healthy diet and lifestyle they target specific health goals providing every cell the most appropriate and optimal nourishment. These herbal supplements do not have any harmful side effects that might disturb physical health unlike synthetics. For every synthetic drug present there is an alternative herbal drug. Man in his everlasting search for cure of serious illnesses, at last finds his way to our indigenous medicine.

Importance

Ayurveda is a traditional system of medicine using a wide range of modalities to create health and wellbeing. The main aspire of Ayurveda health care is to restore the physical mental and emotional balance in patients, thus improving the health, preventing disease and to treat any current illness. The number of patients looking for alternate and herbal therapy is growing exponentially. Thus, the herbal medicines are now in great demand in the developing world for primary healthcare not only for its inexpensiveness but also for better cultural acceptability; better compatibility with the human body and minimal side effects.[17,15]

Formulation of herbal products[11]

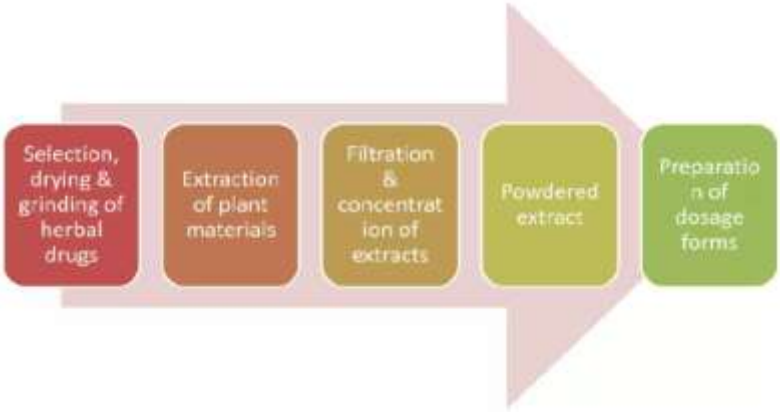


Figure 4: Steps in herbal drug formulation.

Types of conventional herbal formulation

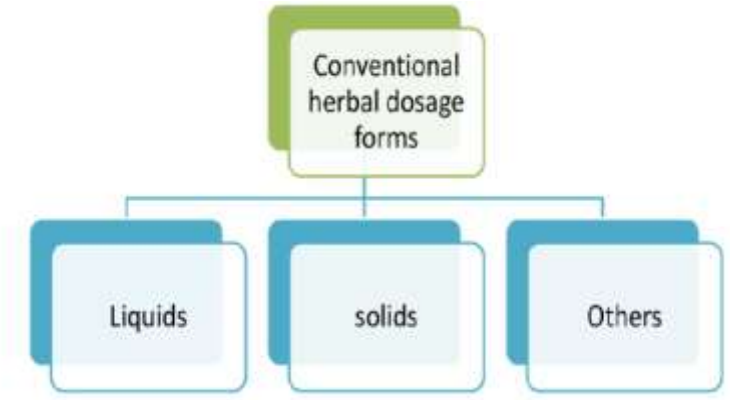


Figure 5: Types of conventional herbal formulation.

Herbal tablets

Herbal Tablets are the solid dosage form of powdered herbs, herbal extracts or their constituents prepared by moulding or compression, blended with excipients & compressed to form a defined size & shape. Tablets are usually circular in shape and may be flat or biconvex.

Figure 6: Herbal tablets.

Preparation methods

1. **Direct compression**
2. **Wet granulation**
3. **Dry granulation**

Herbal drugs for the diabetes mellitus

The Ayurvedic medical system, as described in ancient Indian texts such as Charak Samhita, Mahdhav Nidan, and Astang Sanghra, includes a list of about 600 plants with reputed anti-diabetic properties. A variety of plant-derived active compounds representing numerous phytochemicals have consistently demonstrated hypoglycemic activity, implying their potential utility in the treatment of diabetes mellitus.[17,19]

Allium cepa, *Allium sativum*, Aloe vera, *Berberis aristata*, *Cajanus cajan*, *Coccinea indica*, *Caesalpinia bonducella*, *Cyperus rotundus*, Ficus bengalensis, and Ficus bengalensis are among the most effective and widely studied Indian plants in relation to diabetes. *Momordica charantia*, *Gymnema sylvestre Sacred ocimum*, *Marsh Pterocarpus*, *Syzygium cumini*, *Swertia chirayita Terminalia chebula*, *Terminalia belerica Tinospora cordifolia*, *Trigonella foenum-graecum*, *Phyllanthus emblica*, *Annona squamosa*, and other species are included.[18-21]

Herbal medicines have been used to treat diabetes, either alone or in combination with other medications. Polyherbal formulations have the potential to increase pharmacological activity while reducing individual herb concentrations, thereby minimizing adverse effects. Rather than individual components, plant-based formulations and combined extracts of multiple plants have been used as drugs.

Here is example of some herbs which have anti diabetic properties

1. ***Withania coagulans*: (Paneer ke phool)**

Paneer flower which is also known as Paneer Doda and Indian Rennet. Paneer flowers are native to India, Pakistan and Afghanistan. It is known for its medicinal properties and proves to be very helpful in fighting diabetes.

How does paneer ke phool help in managing diabetes?

Paneer Phool heals pancreatic beta cells, resulting in better insulin utilization. It can effectively help manage high blood sugar levels when consumed on a daily basis, even in

small amounts. It has the ability not only to regulate insulin levels within our cells, but also to rejuvenate the pancreatic beta cells, which are responsible for insulin production. The beta cells in the islets of Langerhans are frequently impaired in diabetics. Consequently, those with type-2 diabetes are unable to generate insulin internally, necessitating an external source. This is where the significance of paneer Ke Phool or paneer doda becomes evident.[22]

Figure 7: Paneer ke phool.

Paneer Ke Phool is typically consumed in the form of a kadha. An alternate method for consuming Paneer Ke Phool in the form of tablet by drying and using it in the tablet formulation.

2. *Syzygium cumini*: (Jamun seeds)

Antidiabetic, antioxidant, hypolipidemic, ulcer prevention, nitric oxide scavenging, free radical scavenging, and radioprotective properties have been attributed to various parts of the Jamun tree. Both in vivo and in vitro studies have shown that it has anti-diabetic properties, making it useful for diabetics who can benefit from its fruit and leaves28. The fruit promotes the conversion of carbohydrates into energy and aids in blood sugar regulation. Because of its low glycaemic index, diabetic patients are advised to consume Jamun during the summer months, as it can alleviate symptoms such as excessive urination and thirst. Diabetes management has been greatly aided by extracts from the leaves, seeds, and bark.[23,25]

Figure 8: Jamoon seeds.

Prediabetes, a metabolic condition in which blood glucose levels are slightly elevated but do not reach the diabetes threshold, is treatable. Jamun seeds, both dried and powdered, have long been used in India to help maintain healthy blood sugar levels. Jamun contains Jambolin, an important glycoside that inhibits the conversion of starch into sugar, thereby aiding in blood sugar control.

A study on rats was conducted to assess the lipid-lowering and anti-diabetic effects of herbal medication and its main ingredient, Jamun seed, in four groups: control, glibenclamide, petroleum ether extract of Jamun seed powder (PESE), and herbal medicine (HM-01).[24,26,27]

3. *Tinospora cordifolia*: (Giloy)

Giloy is known as a 'Madhunashini' in Ayurveda, which means "sugar destroyer." It aids in the production of insulin, which in turn regulates blood sugar levels. Giloy is also beneficial for diabetes complications such as ulcers and kidney problems.

Figure 9: *Tinospora cordifolia.*

Giloy for diabetes – How does it work?

According to some experts, giloy extract may have hypoglycaemic and anti-diabetic properties. Insulin is a peptide hormone that aids in blood sugar regulation.

Giloy, an Ayurvedic herb, can help the body produce insulin naturally, which can help with diabetes management. Giloy can also help with diabetes management by improving the digestive system and gut health. This is due to the fact that digestive health determines how well our bodies absorb nutrients from food. Giloy has the potential to reduce insulin resistance, improve glucose utilization, reduce oxidative stress, and boost cell antioxidant status. All of this has the potential to lower blood glucose levels.[18]

4. *Allium sativum*: (Garlic)

This is a perennial herb that is grown all over India. The pungent Odor is caused by allicin, a sulphur-containing compound that has been shown to have significant hypoglycaemic activity. This effect is attributed to increased hepatic metabolism, increased insulin release from pancreatic beta cells, and/or an insulin sparing effect. In comparison to sucrose controls, an aqueous homogenate of garlic (10 ml/kg/day) administered orally to sucrose fed rabbits (10 g/kg/day in water for two months) significantly increased hepatic glycogen and free amino acid content, decreased fasting blood glucose, and triglyceride levels in serum.[18]

Figure 10: Garlic.

5. *Azadirachta indica*: (Neem)

This plant's hydroalcoholic extracts exhibited anti-hyperglycaemic activity in streptozotocin-treated rats, owing to an increase in glucose uptake and glycogen deposition in isolated rat hemidiaphragm.

Figure 11: Neem.

This plant not only has anti-diabetic properties, but it also has anti-bacterial, antimalarial, antifertility, hepatoprotective, and antioxidant properties.[19]

6. *Aloe indica royle*: (Aloe vera)

Figure 12: Aloe vera supplements.

Aloe vera is a common plant with numerous applications. Many people are aware of its skin benefits, but it may also have other benefits, such as slowing the progression of type 2 diabetes. Aloe vera users can add its juiced pulp to a drink, such as a smoothie, or take it as a supplement in capsule form.

7. *Mangifera indica: (Mango)*

Although the leaves of this plant are used as an anti-diabetic agent in Nigerian folk medicine, an aqueous extract given orally had no effect on blood glucose levels in normoglycemic or streptozotocin-induced diabetic rats.

Figure 13: Mango leaves.

However, anti-diabetic activity was observed when the extract and glucose were administered concurrently, as well as when the extract was administered 60 minutes before the glucose. The findings suggest that an aqueous extract of Mangifera indica has hypoglycaemic activity. This could be due to a decrease in glucose absorption in the intestine.

8. *Momordica charantia:* (Bitter gourd)

Momordica charantia is widely used in India and other Asian countries as an antidiabetic and antihyperglycemic agent. In various animal models, extracts of fruit pulp, seed, leaves, and the entire plant were shown to have a hypoglycaemic effect. Polypeptide p, isolated *from M. charantia* fruit, seeds, and tissues, had a significant hypoglycaemic effect when administered subcutaneously to langurs and humans.[18,19]

Figure 14: Bitter ground.

In normal and STZ diabetic rats, ethanolic extracts of *M. charantia* (200 mg/kg) had an antihyperglycemic and hypoglycaemic effect. This could be due to the inhibition of glucose-6-phosphatase in addition to fructose-1, 6-biphosphatase in the liver, as well as the stimulation of hepatic glucose-6-phosphate dehydrogenase activities.

9. *Ocimum sanctum:* (Holy basil)

Tulsi is its common name. This plant has been used for medicinal purposes since ancient times. The aqueous extract of *Ocimum sanctum* leaves reduced blood sugar levels significantly in both normal and alloxan-induced diabetic rats. Tulsi's hypoglycaemic and hypolipidemic effects in diabetic rats were demonstrated by significant reductions in fasting blood glucose, uronic acid, total amino acid, total cholesterol, triglyceride, and total lipid.

Figure 15: *Ocimum sanctum.*

On the 15th and 30th days of the experiment, oral administration of plant extract (200 mg/kg) resulted in a decrease in plasma glucose level of approximately 9.06 and 26.4%, respectively. When diabetic rats were compared to control rats, their renal glycogen content increased tenfold, while their skeletal muscle and hepatic glycogen levels decreased by 68 and 75%, respectively.[17-19]

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