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Review on Crude Drug Used in Diabetes Mellitus

Mr. Pratik R. Khandagale[1], Miss. Kalyanee V. Gavande[2], Dr. Amol N. Khedkar[3], Mr. Prajwal R. Bhujbal[4]

[1,4]Student, Department of Pharmaceutical Science, Saikrupa Institute Of Pharmacy, Ghargaon, Ahmednagar, Maharashtra, India -413728
[2]Assistant Professor, Department of Pharmaceutical Science, Saikrupa Institute Of Pharmacy, Ghargaon, Ahmednagar, Maharashtra, India -413728
[3]Principal, Department of Pharmaceutical Science, Saikrupa Institute Of Pharmacy, Ghargaon, Ahmednagar, Maharashtra, India -413728

Abstract:
Approximately 60% of people on the planet utilize traditional medicines made from medicinal plants. This review is on Indian herbal medications and plants, particularly those utilized in India, for the treatment of diabetes. Diabetes is a significant illness that affects people worldwide and from all walks of life. It is turning out to be a serious health issue in India, particularly in the cities. Herbal formulations are recommended because they have fewer side effects and are less expensive than other techniques to lessen the negative effects of diabetes and its secondary complications. A list of herbal medications used to treat diabetes as well as medicinal plants with demonstrated anti-diabetic properties and associated health benefits is compiled. Among them are Momordica charantia Ocimum, Eugenia jambolana, and Allium sativum, Phyllanthus amarus, Withania somnifera, Tinospora cordifolia, Pterocarpus marsupium, Ocimum sanctum, and Trigonella foenum graecum. Free radical damage is one of the etiologic factors linked to the development of diabetes and its consequences, so an antidiabetic molecule with antioxidant characteristics would be more advantageous. Consequently, details regarding these medicinal plants' antioxidant benefits are also provided.

Keywords: Diabetes Mellitus; Herbal Drugs; Extract; Traditional Medicine; Polyherbal

1. Introduction

Diabetes mellitus, a non-infectious endocrine disorder, is typified by a disruption in the metabolism of carbohydrates and is linked to hypoglycemia [1] [2]. It is associated with the development of a number of serious illnesses, including macro-vascular (peripheral vascular disease and coronary heart diseases) and micro-vascular (nephropathy, retinopathy, and nephropathy) [3]. Diabetes mellitus, commonly referred to as "sweet urine" and muscle atrophy, has been linked to the illness. Insulin is a hormone released from the pancreas that keeps blood glucose levels stable. The pancreas produces insulin to maintain the level of glucose when these levels rise. Hyperglycemia is a result of reduced or absent insulin production in diabetic patients [4]. There are three types of diabetes mellitus. type 1, Gestational diabetes mellitus and type 2. Insulin-dependent diabetes mellitus, also referred to as type 1 diabetes mellitus, is caused by the complete failure of the β cell in the pancreatic islets of Langerhans. Insulin non-dependent diabetes mellitus, or type 2 diabetes mellitus, is characterized by a transient loss of β cell

mass caused by a genetic predisposition. It primarily affects obese individuals and is linked to elevated blood pressure and cholesterol levels. Reducing insulin resistance and boosting insulin secretion are the goals of type 2 diabetes treatment. Hyperglycemia is a symptom of gestational diabetes, which affects pregnant women. Typically, it manifests in 2-4% of second- or third-trimester pregnancies[5]. Diabetes mellitus symptoms include blurred vision, slow wound healing, polydipsea, polyuria, polyphagia, fatigue, nausea, and vomiting. In men, impotence is also a symptom of the disease [6].

1.1 Diagnosis of diabetes mellitus

Blood sugar levels can be analyzed to determine the level of diabetes. In a healthy man, blood sugar levels can reach up to 160 mg/dl after a meal and 80 mg/dl during a fast. Various tests, such as the finger prick blood sugar test, fasting blood sugar test, glucose tolerance diagnostic test, and glycohemoglobin, are used to diagnose diabetes in laboratories [6].

2. Pathophysiology of diabetes mellitus

Oxidative stress plays a significant role in diabetes pathophysiology. Oxidative stress refers to the disparity between the generation of reactive oxygen species (ROS) and the ability of enzymatic or non-enzymatic antioxidants to counteract them. Hydroperoxyl, super oxide, peroxyl, and hydroperoxyl are examples of free radicals found in reactive oxygen species. Non-radical species like hydrogen peroxide are also included. Superoxide dismutase, glutathione reductase, trace elements, vitamins A, C, and E, and carotenoids are all found in antioxidants. Oxidation occurs in low density lipoprotein cholesterol the existence of reactive oxygen species, which cause foam cells and plaques associated with arterial sclerosis to form by binding to the hunter receptor in scavenger cells. These ROS have the ability to stimulate a number of harmful pathways, which are crucial in the development of diabetes mellitus. The electron transport chain, the glucosamine pathway, the sorbitol aldose reductase pathway, and the stimulation of protein kinase C are a few significant pathways. Induction of these pathways and their mode of action can result in the development of amylin, lipid peroxidation, atherosclerosis, programmed cell death, and failure of the function of the pancreatic β cell. It has been demonstrated that the negative regulator for these sequence-specific DNA binding factors, kelch like ECH associated protein 1, and nuclear factor erythroid derived 2 like 2, have a significant protective mechanism for cells against oxidative stress [7].

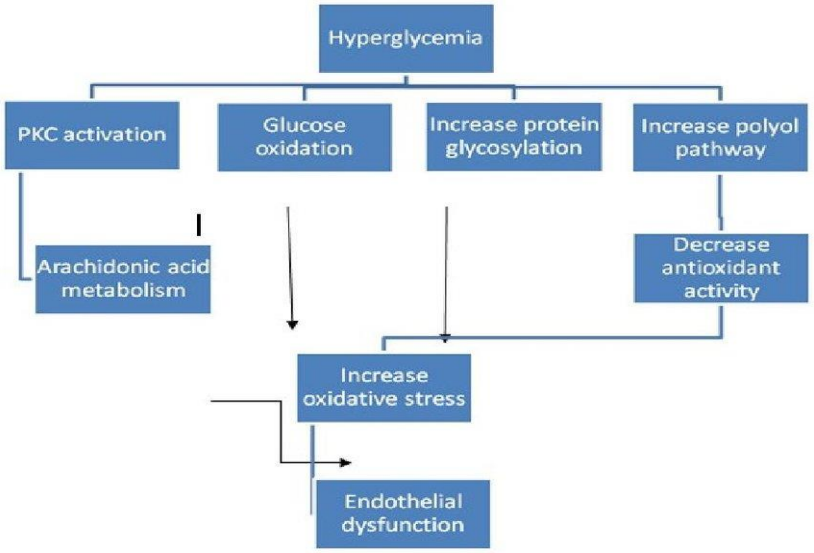

Figure 1: Pathophysiology Of Diabetes Mellitus

2.2 Anti-diabetic drugs

Diabetes mellitus can be avoided by controlling blood sugar levels with a variety of medications, getting to alternate yoga poses, workout regimens, or dietary plans [8]. Insulin treatment for type 1 diabetes and other oral hypoglycemic medications such sulphonylureas, thiazolidinediones, and peptide analogs for type 2 diabetes are currently the available therapies for diabetes mellitus [4] [9].

2.3 Herbal Remedy:

The biggest question facing medical professionals today is how to treat diabetes mellitus without causing any negative side effects. Approximately 800 medicinal plants are used to prevent diabetes mellitus, according to the World Ethanobotanical Society. Only 450 medicinal plants have been shown in studies to have anti-diabetic qualities, of which 109 have a full mode of action. Traditional medicinal plants with their active ingredients and therapeutic qualities were used in the past by both medical professionals and laypeople to treat a variety of illnesses, including diabetes, cancer, and heart disease. In India and China, traditional herbal remedies for diabetes have a long history of use. Numerous books, including Susruta Samhita and Charaka Samhita, are available and explain the phy-topharmacology features of diabetes and its negative effects. [10]Synthetic medications used to treat diabetes have been linked to a number of negative side effects, including nausea, vomiting, dysentery, headaches, alcohol flush, swelling, malignant anemia, and dizziness. Because they have fewer negative effects and side effects than synthetic drugs, herbal medications have been shown to be a better option. Herbal remedies are easily obtained over-the-counter without a prescription. These herbal medications are used to treat serious illnesses. These medications are also used when chemical medications fail to effectively treat a disease. These are safe and natural medications, meaning that Vermas et al. 2018;10(1):1–10; International Journal of Phytomedicine

Table 1: Synthetic Anti-diabetic drugs

Sr.no	Category	Name of Drugs	Brand Name	Mode of Action
1	Insulin	Regular Insulin	Humulin R Apidra Humulin N Novolin N Ultralente	Decrease glucose production and Increase peripheral glucose uptake
	Rapid acting insulin	Insulin glulisine,		
	Intermediate acting Insulin	Isophane Insulin		
	Long acting Insulin	Neutual protamine Hagedorn Extended insulin zinc insulin		
2	Alpha glycosidase inhibitors	Acarbose Miglitol	Precose Glyse	Decrease glucose absorption from intestine
3	Biguanides	Metformin, Phenformin	Glucophage DBI	Decrease insulin resistance
4	Meglitinide	Repaglinide Nateglinide	Prandin Starlix	Insulin secretogogues
5	Sulfonylurea (First generation agents)	Tolbutamide Chlorpropamide Glipizide Glimepiride	Orinase Diabinese Glucoltrol Amaryl	Block the ATP sensitive potassium channels
6	Thiazolidinediones	Rosiglitazone	Avandia Actos	Avandia Actos

		Pioglitazone		
7	Peptide analogs [Injectable incretin mimetics Glucagon like peptide -1 (GLP-1) Gastric inhibitory peptide analogs Injectable Amylin analogues]	Exenatide Sitagliptin Saxagliptin linagliptin Pramlintide	Byetta Januvia Onglyza Tradjenta Symlin	Increase incretin levels which inhibit glucagon release and increases insulin secretion
8	Glycosurics	Canagliflozin	Sulisent, Invokana	Inhibit reabsortion of glucose in the kidney and lowerblood sugar level

Drugs from the herbal world treat a person's illness and cure them permanently, unlike those from the synthetic world, which do not. Natural herbs, fruit and vegetable extracts, and herbal formulations are used to treat a variety of illnesses without causing side effects. However, chemical drugs are also manufactured artificially and can have adverse effects. When considering allopathic medicines, herbal formulations are more affordable. Environmentally friendly are herbal formulations. A natural product is used to make herbal formulations, whereas chemically and chemically modified natural products are used to make allopathic medicines. Allopathic medicines must be prescribed, but herbal formulations can be purchased without one [11,12]

2.4 Traditional herbal Anti diabetic drugs

The anti-diabetic properties of medicinal plants and herbs are currently being utilized in ex- tract forms. Medicinal plant extracts have been shown in numerous clinical investigations to exhibit anti-diabetic activity and to restore the function of pancreatic β- cells [13].

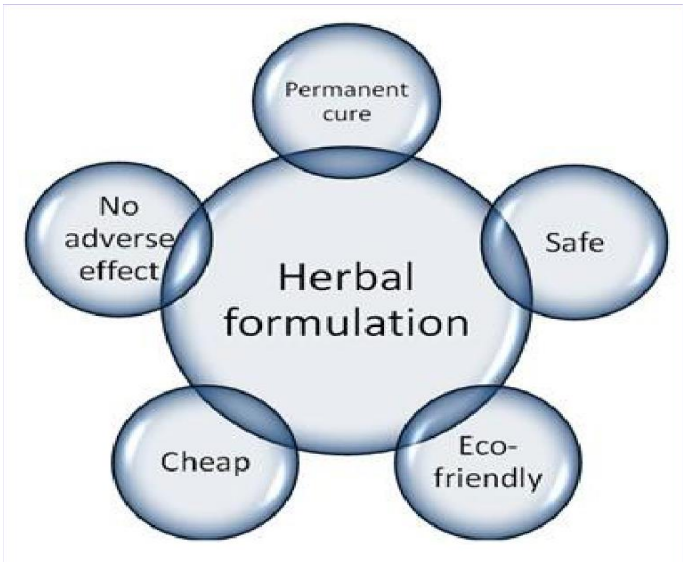

Fig. 2 Advantages of Herbal Formulation

TABLE 2: Herbs and their biological source, family and chemical constituents

Sr. No.	Common Name	Biological Source	Chemical Constituents
1	Garlic	Dried leaves of Allium sativum (Liliaceae)	Glibenclamide allicin, alliin, diallyl sulfide, diallyl disulfide, diallyl trisulfide, ajoene, and S-allyl-cysteine
2	Aloe	dried latex of leaves of Aloe borbadensis (Liliaceae)	Anthraquinones chromone and its glycoside derivatives
3	Neem	consists of the fresh or dried leaves and seed oil of Azadirachta indica (Meliaceae)	stembark ethanol fraction nimbin, nimbanene, 6-desacetylnimbinene, nimbandiol, nimbolide, ascorbic acid, n-hexacosanol and amino acid, 7-desacetyl-7-benzoylazadiradione
4	Mustard	genus of plants in the cabbage Brassica juncea (Cruciferae)	Glucosinolate erucic, arachidic, α-linolenic, oleic, and palmitic acids
5	Papaya	succulent fruit of a large plant of Carica papaya (Caricaceae)	Trimethylamine alkaloids, glycosides, tannins, saponins, flavonoids
6	Vinca (Sadafuli)	dried entire plant of Catharanthus roseus (Apocynaceae)	Alloxan an indole nucleus (catharanthine), and a dihydroindole nucleus (vindoline)
7	Coriander	dried, ripe fruits of Coriandrum sativum (Apiaceae)	alloxan, linalool, limonene, camphor, and geraniol.
8	Jamun	Riped fruit of Eugenia jambolana (Myretaceae)	ferulic acid and malvidin flavonoids, phenolic, anti-inflammatory, anthocyanins, gallic acids, tannins, phenols, alkaloids, ellagic acid, glycoside, isoquercetin, kaempferol, myricetin, tannins
9	Gudmar	woody climbing plant of Gymnema sylvestre (Asclepidaceae)	streptozotocin. Alkaloids, phenolics (tannins), flavonoids, triterpenoids and steroids
10	Mango	Dried fruit of Mangifera indica	Alloxan amino acids include

		(Anacardiaceae)	lysine, leucine, cysteine, valine, arginine, phenylalanine, and methionine
11	Bitter gourd	Dried leaves of momordica (Cucurbitaceae)	Momordic triterpene glycosides, phenolic acids, flavonoids, essential oils, fatty acids, amino acids, sterols, saponins and proteins;
12	Tulasi	Dried seed of propagated Ocimum sanctum (Labiateae)	Streptozotocin, oleanolic acid, ursolic acid rosmarinic acid, eugenol carvacrol, linalool, and β-caryophyllene
13	Gulvel	Dried male and female flowers of Tinospora cardifolia (Menispermaceae)	Diterpene alkaloids, glycosides, steroids, phenolics, aliphatic compounds, polysaccharides, leaves are rich in protein (11.2%), calcium and phosphorus
14	Bael	riped fruit of Aegle marmelos (Rutaceae)	Alloxan coumarin, xanthotoxol, imperatorin, aegeline, and marmeline.
15	Onion	Dried root of Allium cepa (Alliumcepa)	allyl propyl allicin, quercetin, fisetin, other sulphurous compounds: diallyl disulphide and diallyl trisulphide
16	Baby water (Tindora)	Fruit of Coccinia indica (Cucurbitaceae)	Magnesium Chloride, Calcium Chloride, Potassium Bicarbonate Triterpene
17	Turmeric	Whole plant of Curcuma longa (Zingiberaceae)	Curcumin, Volatile oil, Starch and other related Curcuminoids
18	Senna	Flower, buds, leaves, steam of Cassia auriculata (Leguminosae)	glycosides, glucosides, sennoside, calcium oxalate, sterol and resin Palmitic acid

3. Therapeutic role of crude drugs in DM:

3.1 Allium sativum(Garlic)

Roles: Garlic ethanol extract (10 ml/kg/day) frequently demonstrates hypoglycemic action [2]. Garlic extract proved to be more effective than glibenclamide, an anti-diabetic medication [15]. Rats given STZ

were shown to exhibit anti-diabetic effects from ethanol, ethyl acetate, and petroleum ether extract. Several medicinal properties of garlic include anti-platelet, antibacterial, blood pressure-lowering, and cholesterol-lowering effects [16]. Due to enhanced hepatic glucose metabolism or increased insulin usage, garlic and its derivatives have hypoglycemic activity, which further reduces the risk of diabetes complications.

Fig. Garlic

3.2 Aloe borbadensis (Aloe):

Roles: A dose of 150 mg/kg of body weight taken orally after taking an aqueous extract of aloe vera significantly lowers blood glucose levels [18]. Aloe Vera gel has a number of medicinal benefits, including anti-diabetic and antioxidant properties. It also causes a four-fold increase in glutathione levels in diabetic rats [4]. In diabetic patients, aloe vera lowers blood glucose levels. Additionally, it increases the body's tissues' receptivity to insulin, increasing the drug's efficacy. Aloe vera's active ingredients assist in lowering high blood pressure as well.

Fig. Aloe

3.3 Azadirachta indica (Neem):

Role: Azadirachta indica ethanolic and aqueous extracts lower blood sugar levels. Neem leaf extract has been shown to widen diabetes patients' blood vessels, and neem leaves and seed have been shown to lower the dosage of insulin that must be given to a diabetic patient**.**

Fig. Neem

3.4 Brassica juncea (Musturd):

Roles: It's commonly used as a spice in a variety of dishes. In rats given alloxan to induce diabetes, the aqueous seed extract was shown to have blood sugar-lowering properties. Hypoglycemic action is demonstrated by ex- tract doses of 250, 350, and 450 mg/kg [18]. Beta carotene, one of the many health-promoting antioxidants found in mustard greens, can protect your skin and reduce diabetes risk factors**.**

Fig. Mustard

3.5 Carica papaya (Papaya):

Roles: In alloxan-induced diabetic rats, extract from seeds and leaves demonstrates lowering blood sugar, lipid levels in the body, and wound healing activities. 19] Papain and chymopapain, two enzymes found in papayas, can aid in the digestion of proteins, lipids, and carbs into forms that are easily absorbed, hence reducing blood sugar rises.

Fig. Papaya

3.6 Catharanthus roseus (Sadafuli) :

Roles : In rats given alloxan to induce diabetes, methanolic extract of leaves and twigs demonstrates a drop in blood sugar levels. Animals' blood sugar levels were found to be lowered by oral administration of a 500 mg/kg dose of extract from leaves and twigs [18]. Catharanthus roseus works by increasing the β cells of Langerhans' ability to synthesize insulin [2].

Plants are used to treat diabetes and cancer; their roots are used to treat fevers; their paste is used to treat septic wounds; their juice is used to treat blood dysentery; and their leaves are used to treat menorrhagia. While latex is helpful for scabies, the leaf decoction is good for babies who have gripping pain**.**

Fig. Sadafuli

3.7 Coriandrum sativum(Coriander) :

Roles : It is frequently used as a spice in a variety of foods. In diabetic rats induced with alloxan, 200 mg/kg seed extract often increases the activity of Langerhans β cells, lowers serum sugar, and stimulates the pancreatic β cells to produce insulin.The extract of Coriandrum sativum exhibits insulin synthesizer and blood sugar-lowering properties [2]. Numerous investigations involving animals have confirmed that coriander seeds have a hypoglycemic effect on humans**.**

Fig. Coriander

3.8 Eugenia jambolana(Jamun):

Roles : Patients with diabetes are treated with a 200 mg/kg extract of dried seeds [21]. Through direct inhibition of intestinal glucose loading, insulinotropic activity, and correction in the carbohydrate metabolic pathway following inhibition in the hyperglycemia induced apoptosis process, jambolana demonstrates a potent antidiabetic effect in experimental model rats

Fig. Jamun

3.9 Gymnema sylvestre (Gudmar):

Roles: It is commonly known as Gudmar, which means "sugar destroy-ing." G. sylvestre leaf extract (3.4/13.4 mg/kg) significantly lowered blood sugar levels in rats given streptozotocin. For the treatment of diabetes, it is primarily utilized in Indian ayurvedic medications. Alkaloids, flavonoids, saponins, and carbohydrates are G. Sylvester's active ingredients. Moreover, it is employed in the management of inflammation, cancer, and a variety of microbial diseases [20]. It lowers blood sugar by increasing insulin secretion and shielding pancreatic cells from damage brought on by free radicals.

Fig. Gudmar

3.10 Mangifera indica (Mango):

Roles : In alloxan-induced diabetic rats, oral administration of an aqueous extract did not alter blood glucose levels, despite the leaves extract (250 mg/kg) demonstrating anti-diabetic activity.Twenty [20] Mangos have a high sugar content, which means that most of their calories could potentially increase blood sugar levels, which is especially dangerous for diabetics.

Fig. Mango

3.11 Momordica charantia (Bittargourd):

Roles: It is applied to diabetes treatment. It contains lectin, which functions similarly to insulin. A non-protein connected to insulin receptors is called lectin. By affecting peripheral tissues, this lectin lowers blood sugar levels [21]. M. charantia fruit extract (200 mg/kg) exhibits hypoglycemic action. Several compounds found in bitter melon appear to function similarly to insulin and lower blood sugar. According to some research, they may achieve this by increasing the amount of glucose that enters the cells, which subsequently aids in its digestion and storage by the body in the muscles, fat, and liver.

Fig. Bittergourd

3.12 Ocimum sanctum(Tulasi):

Roles: Indian ayurvedic medicines use it to treat a variety of illnesses. Numerous investigations on animals demonstrated that an aqueous extract of Ocimum sanctum leaves (200 mg/kg) exhibited hypoglycemic effects in rats induced by streptozotocin. Additionally, it is used to treat fungal and viral infections, lower stress, treat tumors, and treat gastric ulcers [22, 23]. Variations in blood sugar levels are indicative of it. Because of its potent anti-inflammatory qualities, tulsi is useful in the treatment of diabetes-related conditions like obesity. Numerous studies suggest that tulsi consumption may enhance insulin secretion and pancreatic beta-cell function.

Fig. Tulasi

3.13 Tinospora cardifo (Gulvel)

Roles: For six weeks, oral administration of T. cardifolia root extract (50-200 mg/kg) resulted in a decrease in blood and urine sugar levels in streptozotocin-induced diabetic rats. For the treatment of diabetes, it is primarily utilized in Indian ayurvedic medications. The reduction of body weight is also prohibited by root extract [20] [28–37].

Fig. Gulvel

3.14 Aegle marmelos (Bael):

Roles: Magnesium, which is abundant in barley, is a co-factor for over 300 enzymes, including those that are involved in insulin secretion and glucose metabolism. It is native to India, where different plant parts, including leaves, barks, roots, and fruits, are used in ayurvedic medicine and other medications that treat a range of illnesses. Neem, tulsi, and A. marmelos leaves are combined, dried, and powdered before being given three times a day for fifteen days. Aegle marmelos (100, 200, and 500 mg/kg) is used to treat a variety of diseases, including cancer, various viral diseases, and various micro- bacterial diseases, according to animal studies [24].

Fig. Bael

3.15 Allium cepa (Onion)

Roles: It is referred to locally as "onion" or "pyaz" and is a member of the Alliumcepa family, Liliaceae. The ether soluble and ether insoluble portions of dried onion powder demonstrated antihyperglycemic action. Its chemical component, allyl propyl disulphide, or APDS, inhibits the liver's ability to break down insulin and stimulates the pancreas to produce more insulin, which raises the concentration of insulin and lowers blood glucose levels. In diabetic rats induced with alloxan, essential oil (100 mg/kg)

extracted from red onions frequently exhibits antioxidant, antihyperglycemic, and antitistatin effects. The most effective percentage for treating hyperglycemia and hyperlipidemia is 300 mg/kg Onions are used in the treatment of cancer, diabetes, asthma, and a variety of viral diseases, according to data from numerous clinical trials and animal studies.The Problems With Herbal Remedies in India onions, which support healthy living and immunity while also assisting in blood glucose regulation.

Fig. Onion

4. The Prospects of Herbal Treatments for Type 2 Diabetes

People use a wide variety of herbal medications, and new native drugs are frequently added to modern therapeutics. In developing nations, particularly in rural areas, about 80% of the population relies on conventional medical treatments for their medical needs. A significant amount of the preference for natural products has led to a resurgence of interest in herbal drugs in developed countries. As a result, it's important to distinguish between herbal medications prescribed by a doctor and those that are widely available for people to take at home. Diabetes mellitus is becoming more and more common, which poses a serious threat to human health everywhere. Newly, potent medications have been derived from plants and have been shown to have greater anti-diabetic effects than oral hypoglycemic medications in clinical trials. The discovery of plants with potential human benefits as antidiabetic agents has garnered attention in recent years. Additionally, it might offer proof of the advancement of a novel oral medication for the management of diabetes mellitus.[26]

4.1 Coccinia indica (Tindora):

Fig. Tindora

Roles: stimulate insulin secretion in diabetic strong antioxidant and anti-inflammatory properties that can aid in the treatment or prevention of a wide range of illnesses, from obesity and high blood pressure to diabetes and high cholesterol.

4.2 Curcuma longa (Turmeric):

Fig. Turmeric

Roles: Curcumin demonstrated a glucose-lowering action and reduced the levels of malondialdehyde, insulin resistance, and dyslipidemia in both tissues. remedy for a wide range of ailments, including blood, liver, and stomach issues, viral diseases, and inflammation.

CONCLUSION:

One of the most prevalent endocrine disorders, diabetes mellitus affects millions of people globally. It is a class of metabolic diseases defined by elevated blood sugar levels brought on by deficiencies in either insulin production, insulin action, or both. Research is shifting toward traditionally available medications with low side effects and a wide range of bioactivity that do not relapse due to the rise in resistance and populations of patients at risk, as well as the limited number of commercially available drugs for diabetes that are still available but have numerous side effects and problems like unwanted hypoglycemic effect. The information in this review article may help researchers, scientists, and health professionals create evidence-based herbal remedies to treat various forms of diabetes. A significant part of developing medications and treating the hyperglycemic issue in diabetes mellitus is played by substances and extracts extracted from various natural resources.

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