



# USE OF HERBAL REMEDIES IN MANAGEMENT OF DIABETES AS A COMPLEMENTARY ALTERNATIVE MEDICINE (CAM) THERAPY

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**ABSTRACT:** Diabetes Mellitus or diabetes is considered as one of the major non-communicable disease in the world. Use of conventional anti-diabetic drugs in the treatment of type II diabetes for longer periods has identified with several health problems and negative side effects. Herbal remedies for specially type II and also type I diabetes management have used since ancient times without proper scientific and clinical approach. However, based on several research findings, hundreds of medicinal plants with potent anti-diabetic activity have been identified and their effectiveness in diabetes management is scientifically proven. There is a keen attraction in the world towards the herbal remedies over the conventional drugs as a complementary alternative medicine due to its natural origin, high availability, low cost and other beneficial health benefits. However, due to lack of awareness about herb drug interactions, preparation methods, effective dose and absence of medical consultancy, use of herbal remedies over diabetes management has reported several health controversies.

**Key words:** Diabetes, Anti-diabetic drugs, herbal remedies, CAM therapy, Herb-drug interaction

## INTRODUCTION

Diabetes mellitus (DM) is recognized as an endocrine metabolic disorder that is characterized by the hypoglycaemic condition along with the impaired metabolism of carbohydrates and other energy releasing molecules like proteins and lipids. Around 2.8 % of the global population was suffering from DM in 2011 and this might be more than 5.4 % in 2025 (Shukla et al., 2011). This is considered as a disease condition rather than a disease and highly linked with nephropathy, retinopathy, peripheral vascular disease and the coronary heart disease as long term and short term impacts of exposing into abnormal glucose concentration in the blood stream. Pathological impacts regard to the Diabetes mellitus are basically due to its actions like declining glucose utilization, increasing fat mobilization from the storage tissues and protein depletion in the tissues. The Glucose concentration is maintained in the human body by the combined activity of glucagon and insulin hormones produced in pancreas and due to the zero or inadequate production of insulin, hypoglycaemic condition can be resulted. DM is identified by the analysis of blood sugar level in the blood and it is considered as 80 mg/dl and 160 mg/dl in a normal healthy man at fasting and postprandial state accordingly.

There are three main types of diabetes as type I, type II and gestational diabetes and other types of diabetes as Maturity Onset Diabetes (MODS) and secondary diabetes. **Type I Diabetes** - This condition occurs when the immune cells are self-attacked the beta cells in the pancreas that produce insulin and therefore this is an auto-immune disease. Immune cells can be triggered due to another illness or due to stress and attack on the beta cells in one's body. The survival of these patients depend on regular insulin injections as the body can't produce enough insulin hormone for the normal action. This is considered as Insulin Dependent Diabetes Mellitus (IDDM) and most prevalently diagnosed in children, adolescents and young adults. **Type II Diabetes** - This is a condition occurs when the pancreas produce enough insulin but the body cells can't utilize it. This is happened due to the insulin resistance of the body and eventually the pancreas become unable of producing enough insulin. This is considered as Non-Insulin Dependent Diabetes Mellitus (IIDDM) and most common in groups over 40s and overweight. According to Moradi, et al. (2018), it has shown that around 85 % to 90 % cases in the developed nations and even higher amounts in developing countries are this type II category. **Gestational Diabetes** - This is a temporary hyperglycaemic condition occur in some women during their pregnancy specially during the third trimester due to the hormonal changes linked with the overweight and family history of diabetes. Clinical detection is very much important as it can cause parental morbidity and mortality. According to the American Diabetes Federation, around 4 % of pregnant women can develop this gestational diabetes. **Maturity Onset Diabetes** - This is a mild hyperglycaemic condition and prevalent in early stages of life due to the impaired insulin secretion as there is a genetic inability of converting proinsulin into insulin. **Secondary Diabetes** - This condition

arises as a result of another pre-existing health conditions like down syndrome, cystic fibrosis, pancreatitis and different medical treatments with immunosuppressive, corticosteroids.

Treatment for diabetes includes the use of insulin injections for type I diabetes and synthetic antidiabetic drugs, use of herbal remedies for the control of diabetes and sometimes a combination of both of these categories. There are different side effects that have been identified related with the long term use of synthetic antidiabetic drugs over the herbal remedies which have driven a keen attraction towards the herbal treatments for different diabetic categories. It has identified hundreds of herbs that have the antidiabetic function and most of them are still in the experimental stage. This review includes the possible herbal remedies that can be used based on their antidiabetic function in the treatments of diabetes and their limitations, effectiveness and safety over the conventional antidiabetic drugs and the use of as an effective complementary and alternative medicine (CAM) in diabetes.

## USE OF ANTIDIABETIC DRUGS AND HERBAL REMEDIES FOR DIABETES

### Use of Antidiabetic drugs

For type I diabetes insulin protein or its analogues is the possible treatment. Oral insulin intake is not possible because due to the acidity in the stomach the protein gets easily denatured before it gets absorbed into the bloodstream. The type of insulin and the dosage that has to be injected is decided based on the patient's condition. And for the gestational diabetes, it is also treated basically by using insulin insertion. Oral antidiabetic drugs are available and widely used for the type II diabetes treatments. Treatments for type II initially starts with the diet and exercise and then progressed with monotherapy, dual therapy, multi agent therapy and also then the insulin insertion with the combination of other antidiabetic drugs depend on the glucose concentration reference of the patient (Meneses et al., 2015). And the administration of these drugs is done only under the medical supervision.

Table 1- Summary of antidiabetic drugs, their mode of action, main advantages and disadvantages (Meneses et al., 2015).

Antidiabetic class	Antidiabetic Drug	Mechanism of action	Advantages	Disadvantages
$\alpha$ -glucosidase inhibitors	Acarbose Miglitol Voglibose	Inhibit carbohydrates degradation in intestinal villi	Weight neutral	Gastrointestinal side-effects. Negligible effect on cholesterol Potential elevations in liver function tests
Biguanides	Metformin	Block liver gluconeogenesis. Increase skeletal muscle uptake of glucose. Lower the absorption of glucose in the intestinal mucosa. Increase plasma levels of GLP-1	Long-term safety Weight neutral or loss Low risk of hypoglycaemia	Adverse gastrointestinal effects Probability of lactic acidosis Contraindicated for patients with liver or heart failure
Sulfonylureas	Glicazide Glibenclamide Glimepiride	Increase insulin secretion by activating $\beta$ cell SUR 1	Long-term safety	Risk of hypoglycaemia. Risk of weight gain.
Meglitinides	Nateglinide Repaglinide Mitiglinide	Binds to $\beta$ -cell SUR 1	Faster insulin response	Risk of weight gain. Risk of hypoglycaemia. Complex dosing schedule
GLP-1 receptor agonists	Exenatide Liraglutide	Binds to GLP-1 receptor, causing: increased insulin secretion, delayed gastric emptying, and satiety.	Weight loss. Low risk of hypoglycaemia.	Gastrointestinal side-effects Administration by subcutaneous injections
DPP-4 inhibitors	Sitagliptin Saxagliptin Alogliptin	Increase incretin (GIP and GLP-1) concentrations. Increase insulin secretion.	Weight neutral	Gastrointestinal side-effects

Thiazolidinediones	Pioglitazone Rosiglitazone	Activators of the PPAR $\gamma$ . Increase differentiation of preadipocytes. Increase insulin sensitivity in muscle, hepatic and adipose tissue. Increase glucose uptake in peripheral tissues.	Low risk of hypoglycaemia	Risk of weight gain. Risk of oedema Risk of heart failure.
SGLT2 inhibitors	Dapagliflozin Canagliflozin	Limits renal glucose reabsorption	Weight loss. Low risk of hypoglycaemia	Risk of genitourinary tract infections

### Use of Herbal Remedies

Since prehistoric times the use of herbal remedies for the treatment of diabetes was reported in all over the world. The use of herbal remedies is mostly involved with the Type 2 diabetes and lesser amounts of herbal remedies have been used in the case of type 1 diabetes. There is an increasing attraction towards the herbal remedies over the conventional anti diabetic drugs based on the traditional belief about the herbal medicine as they are safe for the use with minimum negative effects and they are widely available and also they are relatively less expensive (Thikekar et al., 2021). And also their preventive role in disease management along with the therapeutic action has highlighted over the anti-diabetic drugs (Qureshi et al., 2018).

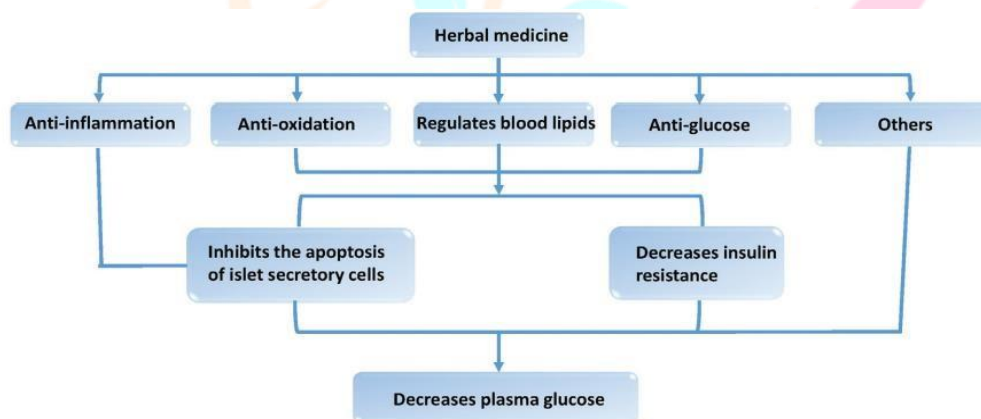


Figure 1- The effect of herbal medicine on diabetes mellitus in different aspects (Pang et al., 2019).

### HERBAL APPROACH TO MANAGE DIABETES

#### Clinically proven remedies

Since many herbs have been identified with an anti-diabetic effect, relatively small amount of plants have its clinical evidences. Following herbal medicines represent the most common and effective herbal medicines available for diabetes based with experimental and clinical evidences.

**Aegle marmelos** – This is known as Bael also and known to have many other health benefits along with its anti-diabetic function. According to Ghorbani (2013), it has shown that a clinical trial done by using 20 type II diabetes which have administrated 5 g of *A. marmelos* leaf powder once day have shown reduction of fasting blood glucose level from 201 mg/dL to 159 mg/dL from 16 days.

**Allium cepa** – This is known as Onion and have shown its anti-diabetic activity in a study with 20 of type II diabetic patients after the oral consumption by regulating the plasma glucose level rise in 37 % 2 hours after ingestion (Ghorbani, 2013). Concentrated puree of *A. cepa* has been shown that it has an effective hypoglycaemic effect by affecting the activity of liverhexokinases and HMG co-enzyme A reductase (Qureshi et al., 2018).

**Nigella sativa** – Seeds of black seeds have used since early period of time due to its hypoglycaemic, hypotensive, hypolipidemic and ant-microbial effect. According to Ghorbani (2013), it has said that a study has proved that 2.5 ml of black seed oil administration twice a day for 6 weeks have reduced fasting blood sugar level and LDL effectively. And also another study has proved that after 40 days of administrating black seed oil to type II diabetic patients has shown a significant increase in insulin and SGOT levels in the plasma.

**Ocimum sanctum** – According to Ghorbani (2013), it has said that a study has proved that administration of 2 g of *O. sanctum* leaf powder once a day for 3 months by using 30 of type II diabetic patients have shown a significant reduction in diabetic symptoms. And also another study has proved that the use of *O. sanctum* powder in 27 type II patients have shown a significant reduction in fasting blood sugar, glycated proteins, total cholesterol, low density lipoproteins, very low density lipoproteins and triglycerides as 21 %, 11 %, 11 %, 14 %, 16 % and 16 % accordingly.

**Salacia reticulata** – This is known as Kothala Himbutu and according to Ghorbani (2013), it has said that a study has proved *S. reticulata* anti-diabetic activity by adding its stem aqueous extraction to the diet as 240 mg per day for 6 weeks have a significant effect on reducing fasting blood glucose level and HbA1c levels in type II diabetic patients. Another study has shown that type II diabetic patients who have received *S. reticulata* tea for 3 months also have shown a considerable change in HbA1c levels.

**Cinnamon** – The active compound in Cinnamon is Cinnamaldehyde which shows the antidiabetic property. According to Qureshi et al. (2018), it has shown that administration of 120 mg and 360 mg of Cinnamon per day for type II diabetic patients have a significant reduction of fasting blood glucose levels and HbA1c levels within them.

**Allium sativum** – This is known as Garlic and the active compound is allicin which has the glucose lowering property. Its action is considered as the active ingredients of garlic readily compete with the insulin site in the liver to release more insulin to the blood flow. And it has proven its potent hypoglycaemic effect by providing 300mg of garlic as thrice per day for 24 weeks that has shown a significant reduction of blood glucose level than the beginning (Qureshi et al., 2018).

**Zingiber officinale** – This is known as Ginger and its hypoglycaemic action is characterized by enhancing glucose uptake and GLUT4. And also that it has potent antioxidant and antiglycating effect. A study has shown that administration of 3 g of dry ginger powder for 30 days for 32 male diabetic patients had a significant reduction in blood glucose, total cholesterol, triglycerides, LDL and VLDL (Qureshi et al., 2018).

**Azadirachta indica** – This is known as Neem and the major components important in the glucose lowering action are the nimbin, nimbidin and nimbnene. And according to Qureshi et al. (2018), study, they have found that administration of 70 % alcoholic extraction of Neem root bark for type II diabetic patients have an effective glucose lowering property at 800 mg/kg dose.

**Aloe vera** – This has a wide range of active compounds that act as anticancer, anti-sclerosis, antioxidant, laxative etc. along with antidiabetic property. It increases the insulin secretion from beta cells as well as increase the production of beta cells. A study has shown that administration of *Aloe vera* for 30 days to type II diabetic patients have a significant effect of lowering blood glucose, total cholesterol and HbA1c levels (Qureshi et al., 2018).

**Momordica charantia** – This is known as Bitter Gourd and has been used in ancient times as diabetes controlling agent. It contains multiple active ingredients like simple phenols, flavonoids, benzoyl derivatives, tannins and carotenoids which have identified in different researches to identify the hypoglycaemic action of Bitter Gourd. A study has shown that the administration of 2.5 g of Bitter gourd powder as a supplement for 52 pre diabetic patients for 60 days had a significant impact on reducing blood glucose level of the participants (Qureshi et al., 2018).

**Trigonella foenum** – This is known as Fenugreek and the use of fenugreek as an antidiabetic agent is identified by its action on the stimulation of insulin production and the secretion and slow down the enzymatic degradation and through that reduce the post prandial glucose level in the plasma. Clinical use of Fenugreek has proved by giving 500 mg of fenugreek seed extraction to 154 type II patients and measuring the fasting and post prandial glucose levels where the glucose levels have significantly reduced (Qureshi et al., 2018).

**Ginseng** – There are 14 Ginseng species have been identified and out of that Korean Ginseng and American Ginseng varieties have been identified for the anti-diabetic activity. Especially the Ginseng roots and the other parts also have been used in anti-diabetic treatments. Most frequent active compounds found in ginseng are the polysaccharides, polyacetylenes and ginsenosides. Mechanism of action has been identified as the activation of peroxisome proliferator-activator receptors and then regulate the glucose and lipid metabolism and the glucose and fatty acid uptake. A study has shown that administration of Ginseng root aqueous extraction to 16 diabetic patients for 2 weeks had a significant reduction of fasting blood glucose levels (Ota and Ulrich, 2017).

**Opuntia spp.** – This is known as Nopal and identified as Prickly pear cactus. The fruit, young and edible cladodes have been used in the medical treatments since ancient times. Nopal contains higher amounts of soluble fibre and pectin which can effectively reduce the glucose uptake within the intestine. A study conducted in Mexico has shown that after the administration of Nopal extraction for 3 weeks, patients with type II diabetes has shown significant reduction in post-prandial blood glucose and increase in serum insulin (Ota and Ulrich, 2017).

**Pterocarpus santalinus** – This is known as Red Sandalwood and contain numerous active ingredients like flavonoids, tannins, saponins and the main ingredient is santalin. Studies have highlighted its antidiabetic, antihelmintic and astringent properties. In traditional medicine drinking water in red sandalwood cups is widely generalized as an effective treatment strategy for diabetes. A study has shown that ethanolic fraction of plant at a dose of 0.25 mg/kg body weight once a day has an effective hypoglycaemic function (Mukhopadhyay et al., 2019).

### **Clinically unproved herbal remedies**

According to Chen et al. (2015), they have found that application of herbal medicines with bitter flavour and cold property have an effective impact on diabetes management. According to the theory of four properties and five flavours, herbal medicine can be classified into several groups. And clinical evidences have been reported that herbal medicine in the bitter flavour and cold property category has the anti-diabetic property by improving insulin secretion at late phase by beta cells and reducing insulin resistance and also reducing fatty acid synthase activity when they are administered as poly herbal medicines. And they have shown its hypoglycaemic action when they are used as single herb treatments basically depend on their active ingredients like alkaloids which is the main compound in around 75 % of herbal medicine in this category and glycosides which is a common compound found in around 56 % of herbs in this category. These alkaloids and glycosides are the main sources of bitter flavour and the cold property of these herbs. The study has reported the effect on blood glucose reduction by using mono herbal formulations from this category identifying the impact of *Rhizoma coptidis*, *Rhubab* and *Momordica charantia* on the blood glucose reduction. The study has also shown the mechanism of action of the herbal medicine in this category as improving insulin secretion and reducing insulin tolerance, regulating sugar metabolism at the liver, reducing glucose uptake, improving glucose utilizing in the tissues. And the study has reported that they can regulate blood glucose level along with the lipid metabolism and with small toxicity and less side effects. Most of the reported herbal medicine with anti-diabetic function are basically in this bitter flavour cold property category and their effectiveness on diabetes management, side effects and dosage are not studied completely yet.

According to Hu et al. (2016), they have highlighted the effectiveness of root of *Helicteres angustifolia* in diabetes management. From previous studies the effectiveness of *H. angustifolia* has been identified as anti-bacterial, anti-tumour, anti-viral, anti-inflammatory. The study has done by using dry *A. angustifolia* root and taking its 70 % alcoholic extraction. Both *in vivo* and *in vitro* studies have done by using Murine C2C12 myoblasts, human hepatocarcinoma cell line HepG2 and mouse 3T3-L1 cells for *in vivo* studies and 6 weeks old Sprague Dewley rats for the *in vitro* study. From the study they have found that all three cell types including adipose, liver and muscle had an increased level of glucose uptake after the treatment of *A. angustifolia* extract. In the acute oral toxicity experiment the results showed that dose of 5 g/kg had not caused any morbid effect and toxicity. And also they have found that 28 days

administration of *A. angustifolia* extract had an impact on reducing fasting blood glucose levels and increased insulin secretion in rat models. And also they have reported that the administration of this plant extract for 28 days can effectively reduce TC, TG, LDL and significant improvement in HDL-C levels in the mouse models. So this study has concluded that the *A. angustifolia* root extract has an anti-diabetic function and it has confirmed by using cell based and animal based assays. But the clinical experiments have not done still to find out the effectiveness of *A. angustifolia* in diabetes treatment as a herbal remedy.

### DRUG FORMULATION

There are many medicinal plants have been identified as useful in diabetes management. Based on the active ingredients found in the medicinal herbs certain drug developments have done in the form of either single herb or as poly herbal formulations. Each formulation has been designed by identifying the herb drug interaction, active ingredients, mechanism of action, effective dose for a particular active ingredient. These formulations are usually designed as supplements for the use along with other conventional anti-diabetic drugs. Therefore, careful medical supervision has to be there in order to prevent serious implications which are common with herbal medicine like gastrointestinal issues, dizziness, diarrhoea, hypoglycaemic levels and organ damages (Modak et al., 2007).

Table 2 – Formulated herbal medicine with hypoglycaemic properties (Modak et al., 2007).

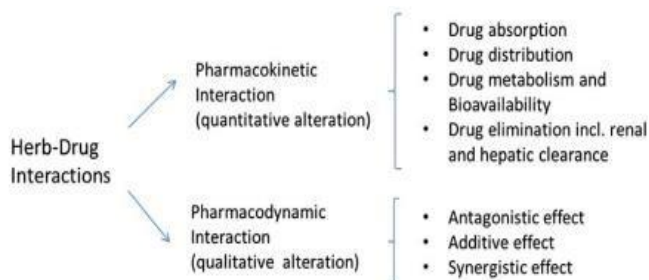
Drug	Company	Ingredients
Bitter gourd Powder	Garry and Sun natural Remedies	<i>Momordica charantia</i> (gourd)
Syndrex Germinated	Plethico Laboretaries	Fenugreek seed extract
Diabecon	Himalaya	<i>Gymnema sylvestre</i> , <i>Pterocarpus marsupium</i> , <i>Glycyrrhiza glabra</i> , <i>Casearia esculenta</i> , <i>Syzygium cumini</i> , <i>Asparagus racemosus</i> , <i>Boerhavia diffusa</i> , <i>Sphaeranthus indicus</i> , <i>Tinospora cordifolia</i> , <i>Swertia chirata</i> , <i>Tribulus terrestris</i> , <i>Phyllanthus amarus</i> , <i>Gmelina arborea</i> , <i>Gossypium herbaceum</i> , <i>Berberis aristata</i> , <i>Aloe vera</i> , <i>Triphala</i> , <i>Commiphora wightii</i> , <i>shilajeet</i> , <i>Momordica charantia</i> , <i>Piper nigrum</i> , <i>Ocimum sanctum</i> , <i>Abutilon indicum</i> , <i>Curcuma longa</i> , <i>Rumex maritimus</i>
Pancreatic tonic 180 cp	Ayurvedic herbal supplement	<i>Pterocarpus marsupium</i> , <i>Gymnema sylvestre</i> , <i>Momordica charantia</i> , <i>Syzygium cumini</i> , <i>Trigonella foenum gracecum</i> , <i>Azadirachta indica</i> , <i>Ficus racemosa</i> , <i>Aegle marmelos</i> , <i>Cinnamomum tamala</i>
Gurmar powder	Garry and Sun natural Remedies	Gurmar ( <i>Gymnema sylvestre</i> )
Diabecure	Nature beaute sante	<i>Juglans regia</i> , <i>Berberis vulgaris</i> , <i>Erythrea centaurium</i> , <i>Millefolium sp.</i> , <i>Taraxacum sp.</i>
Ayurveda alternative herbal formula	Chakrapani Ayurveda	Gurmar ( <i>Gymnema sylvestre</i> ) Karela ( <i>Momordica charantia</i> ) Pushkarmool ( <i>Inula racemosa</i> ) Jamun Gutli ( <i>Syzygium cumini</i> ) Neem ( <i>Azadirachta indica</i> ) Methika ( <i>Trigonella foenum gracecum</i> ) Guduchi ( <i>Tinospora cordifolia</i> )
Diabetes-Daily Care	Nature's Health Supply	Alpha Lipoic Acid, Cinnamon 4 % Extract, Chromax, Vanadium, Fenugreek 50 % extract, <i>Gymnema sylvestre</i> 25 % extract <i>Momordica charantia</i> 7 % extract, Licorice Root 20 % extract
Dia-care	Admark Herbals Limited	Sanjeevan Mool; Himej, Jambu beej, Kadu, Namejav, Neem chal
Epinsulin	Swastik Formulations	vijaysar ( <i>Pterocarpus marsupium</i> )
Diabeta	Ayurvedic cure - Ayurvedic Herbal Health Products	<i>Gymnema sylvestre</i> , <i>Vinca rosea</i> (Periwinkle), <i>Curcuma longa</i> (Turmeric), <i>Azadirachta indica</i> (Neem), <i>Pterocarpus marsupium</i> (Kino Tree), <i>Momordica charantia</i> (Bitter Gourd), <i>Syzygium cumini</i> (Black Plum), <i>Acacia arabica</i> (Black Babhul), <i>Tinospora cordifolia</i> , <i>Zingiber officinale</i> (Ginger)

### HERBAL REMEDIES AS COMPLEMENTARY ALTERNATIVE MEDICINE (CAM) THERAPY

Complementary Alternative Medicine in diabetes is identified as the use of herbal medicine along with the conventional anti-diabetic drugs in order to have an effective response instead of using them alone. There is a significant increase in the use CAM in usual therapeutic treatment regimen basically due to their natural origin, cost effectiveness, other health benefits rather than reducing the blood glucose only. But there can be potential risks associated with this type of treatment methods due to false diagnoses, overload doses and continuous administration. Preparation defects, plant identification defects, herb drug interaction (Kesavadev et al., 2017).

According to Kasole et al. (2019), they have shown that 58.6 % of total sample of type II diabetes patients are using herbal medicine as a CAM along with the conventional drugs. And also they have found that 32.1 % of them are using these medicine based on family and friends' recommendations not by consulting their health care providers. According to another study done by Alqathama et al. (2020), they have found that 71.4 % of their sample of type II patients are not using herbal medicine with proper consultancies. This condition has caused a serious possibility of creating serious herb drug interactions with several side effects.

Herb Drug interactions can be happened either pharmacodynamically or pharmacokinetically. And it can cause antagonistic or synergistic effect or it can cause changes in the drug levels in the body creating either positive or negative impact when two types of drugs are getting interacted. When considering herb drug interactions in pharmacokinetics, it can be affect gastrointestinal absorption by changing the bioavailability and it can affect drug distribution within the body, drug metabolism and drug excretion. When considering the herb drug interactions in pharmacodynamically, it has when the herbs with different structural and chemical compounds get interfere with physiological and biological processes of other drugs indirectly or directly to have antagonistic or synergistic effects (Singh and Zhao,



2017).

Figure 2- Mechanism of action in herb- drug interactions (Verma et al., 2018).

Active compounds in herbal medicine usually induce or inhibit the cytochrome enzymes and transport proteins through that they affect cytochrome pathway in which most of the oral hypoglycaemic drugs are metabolized. This is why there have many evidences that prove this herbal remedies and the conventional drugs can be interacted when they are administrated simultaneously. The effect can be either inductive or inhibitory for hyperglycaemic level in the blood. There are many herbal plants which interact with other drugs and careful concern and awareness of herb drug interactions is vital when following CAM therapy for an effective and safe outcome (Thikekar et al., 2021).

**Aloe vera** – This has identified as potential blood glucose lowering agent and also identified its herb drug interaction with common anti-diabetic drugs. The interaction of *A. vera* with glibenclamide which is a sulfonylurea has been reported as a synergetic activity where that drug's hypoglycaemic function is elevated in the combination with *Aloe vera* (Verma et al., 2018).

**Ginseng** – This is also known as a potent hypoglycaemic agent and mode of action has identified as similar to metformin. A combination of ginseng and metformin has shown a synergetic effect in elevating plasma insulin level (Verma et al., 2018).

**Ginger** - The herb drug interaction of ginger and glibenclamide has been identified. By administrating 25 mg or 50 mg of ginger extract along with 5 mg of glibenclamide to mouse has shown 26 % and 25 % reduction in fasting blood glucose levels according to the ginger extract dose. But there was only 7.9 % reduction in FBG level when glibenclamide used alone. This has identified as a synergetic interaction between herbs and drugs (Verma et al., 2018).

**Fenugreek** – Interactions of fenugreek and other chemical drugs have been identified by using rat models in several studies. A study has shown that administration of 150 mg/kg of fenugreek extract along with 100 mg/kg of metformin has an additive effect in lowering blood glucose level in 20.7 % rather than using metformin alone (Verma et al., 2018).

**Garlic** – A study has shown herb drug interaction of garlic along with metformin in a synergetic way. Administration of 25 mg or 50 mg per kg along with metformin for 28 days to streptozocin induced rats have shown that there is a significant reduction of plasma glucose, improvement of body weight where the weight loss is a major side effect of using metformin alone (Verma et al., 2018).

## CONCLUSION

Before the use of synthetic anti-diabetic drugs to treat diabetes, especially in developing countries and in rural areas the use of herbal remedies was widely generalized. However, with the understanding of potent side effects of long term use of conventional drugs used to treat type II diabetes, use of herbal remedies now become popular in worldwide. Use of herbal remedies and the effectiveness of those plants for diabetes is scientifically proved by different studies. There are hundreds of medicinal plants which have identified with potent anti-diabetic activity but the misuse of these herbs as a treatment for diabetes without medical supervision has caused several serious side effects like hypoglycaemic condition, organ damages. The use of herbal medicine as a complementary alternative therapy along with the conventional drugs with lower doses for an effective outcome in the diabetes management process is still developing. Though there are many herbal plants have been identified with antidiabetic function small amounts are only tested in clinical trials by using human. The advanced identifications about the herb drug interactions, mechanisms of actions of the herbs have to be performed in order to develop effective CAM therapies that can avoid the side effects of both drugs and the herbal constituents as a novel treatment and management strategy for diabetes.

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