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POTENTIAL HERBAL DRUGS FOR TREATMENT OF DIABETES MELLITUS

***Chaudhari Yogesh[1], Dr. Jain Vandana[2], Ansari Imtiyaz[3], Dr. Kanase Vanita[4] and Sorte Rajeshwari[5]**

[1,3,4,5]*Department of Pharmacology, Oriental College of Pharmacy, Navi Mumbai, Maharashtra, India.
[2]Department of Pharmacognosy, Oriental College of Pharmacy, Navi mumbai, Maharashtra, India.

***Corresponding Author: Chaudhari Yogesh**
Department of Pharmacology, Oriental College of Pharmacy, Navi Mumbai, Maharashtra, India.

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ABSTRACT
Diabetes mellitus is emerging as major health problem.69% adults of developing countries and 20% of developed countries are susceptible to diabetes. Drawbacks of insulin therapy are like local pain, inconvenience of multiple injections, insulin edema, lipohypertropy, insulin allergy, resistance and above all of this are weight gain. Oral hypoglycemic agents like Sulphonylureas (Glibenclamide, Glipizide, Gliclazide), Non- Sulphonylureas (Nateglinide, Repaglinide),. WHO in 1976 officially recognized importance of traditional medicine as source of primary health care by globally addressing its traditional medicine programme. India being the botanical garden of the world, is the largest producer of medicinal herbs. 21,000 plants are listed by WHO, used for medicinal purposes around the world. This review covers pharmacological accounts of some plants with antidiabetec potential. Herbal drugs are the oldest known healthcares available to mankind, enlisted in naturopathic, ayurvedic, homeopathic and other medicine systems obtained from natural sources. Herbal drugs becomes advantageous over allopathic drugs due to their safety, low cost, complete accessibility with enhance tolerance. There is more exploration of antidiabetic potential of new plants/herbs *Beta vulgaris L, Butea manosperma, Cynodon dactylon,, Bombax ceiba L Glycyrrhiza uralensis Morus indica. L, Nigella saliva, Morus inignis L. Murraya koenigii L. Ocimum ratissinuim Psacalium decompositum, Phyllanthus sellowianus, Urtica dioica*.

KEYWORDS: Antidiabetic, Traditional Medicine, Allopathic Drugs, Insulin Hormone, Herbal Drugs.

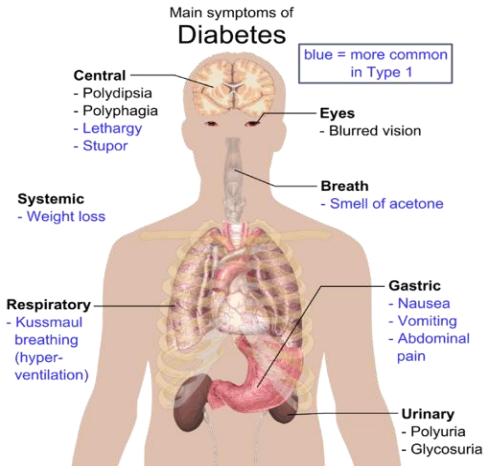
INTRODUCTION
Diabetes mellitus is been recognized has antiquity. It currently affects as many as 285 million people worldwide and results in heavy personal and national economic burdens. Considerable progress is been made in orthodox anti-diabetic drugs. However, new remedies are still in great demand because of the limited efficacy and undesirable side effects of current orthodox drugs. Nature is an extraordinary source of anti-diabetic medicines. Medicinal plants is been used since ancient times for the treatment and management of diabetic mellitus (DM) in traditional medicine systems of many cultures throughout the world recently, medicinal plants continue to play an important role in the management of DM, especially in developing countries, where many people do not have access to conventional anti-diabetic therapies. In developed countries, the use of anti-diabetic herbal remedies has been on the decline because of the introduction of insulin and synthetic oral hypoglycemic drugs during the early part of the 20th century. However, recently in the developed countries, there has been the resurgence of interest in medicinal plants that exhibit hypoglycemic property. The renewed interest in herbal anti-diabetic remedies in developed countries is believed to be motivated by several factors that include: adverse reactions, high secondary failure rates and cost of conventional synthetic anti-diabetic remedies.[1] Recently, the World Health Organization (WHO) recommended the use of medicinal plants for the management of DM and further encouraged the expansion of the frontiers of scientific evaluation of hypoglycemic properties of diverse plant species. Consequently, current estimates showed that over 70% of the Global population applies resources derived from traditional medicine for the management and alleviation of DM and its complications exponential growth in the field of herbal medicine and these drugs are gaining popularity both in developing and developed countries because of their natural origin and less side effects. Many traditional medicines in use are derived from medicinal plants, minerals and organic matter. The World Health Organization (WHO) has listed 21,000 plants, which are used for medicinal purpose around the world.[2]

Diabetes
Diabetes is a metabolic disorder; it is mainly caused by dysfunction of the β cells of the pancreas. This in turn leads to decreased production of the hormone insulin

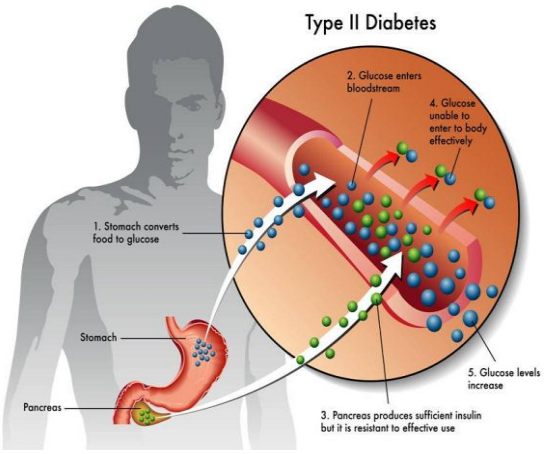
and/or increased resistance to the action of insulin in the peripheral tissues1.

Diabetes can be categorized into two types:
Type-I and
Type-II.

TYPE-I DIABETES
Diabetes or juvenile-onset diabetes develops when the body's immune system damages and destroys the pancreatic β cells that produce the blood glucose regulating hormone insulin. To survive with type 1 diabetes must need to have an exogenous delivery of insulin hormone. This form of diabetes usually attacks children and young adults, although the onset of the disease may occur at any age2. In adults, type 1 diabetes accounts for about 5% of all diagnosed cases of diabetes.[3]



Type I diabetes



Type II diabetes

TYPE-II DIABETES
Type-II diabetes accounts for about 90% to 95% of all diagnosed cases of diabetes. African Americans, Hispanic/Latino Americans, American Indians and some Asian Americans are at particularly high risk for type 2 diabetes, along with its complications and are also being diagnosed, although still rare, as children and adolescents.[4]

Strategy for Treatment of Diabetes
Normally as possible without causing hypoglycemia. Can usually be accomplished with diet, exercise and use of appropriate Allopathic treatment For Diabetes.

Insulin therapy

1. Insulin is a hormone made by the pancreas that allows your body to use sugar (glucose) from carbohydrates in the food that you eat for energy or to store glucose for future use. Insulin helps keeps your blood sugar level from getting too high (hyperglycemia) or to

Allopathic Treatment for Diabetes

DRUG CLASS	INDIVIDUAL DRUG
Sulfonylureas	**1st Genration** 1.Tolbutamide 2.chloropropamide **2nd Genration** 1. Glipizide 2. glyburide
Meglitinides	Nateglinide Repaglinide
Biguanides	1. Metformin
Thiazolidined iones (TZDs)	Pioglitazone Rosiglitazone
Alphaglucosidas inhibitors	Acarbose miglitol

Fig. 1: Classification of allopathic antidiabetic medicines[3, 4]

Disadvantages of Insulin.

1. Can cause weight gain.
2. Can be expensive.
3. Insulin therapy is like to cause local pain, inconvenience of multiple injections, insulin edema, insulin allergy, resistance and above all of this are weight gain.

Affect its components, as will how and when it was harvested and processed. For the reasons described in the previous section, herbalists prefer using whole plants rather than extracting single components from them.

4. Whole plant extracts have many components. These components work together to produce therapeutic effects and also to lessen the chances of side effects from any one component.
5. Several herbs are often used together to enhance effectiveness and synergistic actions and to reduce toxicity. Herbalists must take many things into account when prescribing herbs.

For example, the species and variety of the plant, the plant's habitat, how it was stored and processed, and whether or not there are contaminants.

MATERIALS AND METHODS

***1. Gymnema Sylvester* R.Br (Gurmar booti)**[7,8]
Family: Apocynaceae
Genus: *Gymnema*
Species: *G. Sylvester*
Chemical constituents
Dried leaves containing: Resin, parabin, triterpene glycoside (gymnemic acid 6%), peptide gurmarin), alkaloids (gymnamine), lupenol, quercitol, coloring matter and anthraquinones.
Bark containing: Calcium and starch.
Alcoholic extract: Saponin.

Mechanism of Action[19]
There are some possible mechanisms by which the leaves and especially Gymnemic acids from *G. Sylvester* to shows the hypoglycemic effects are -
1. It increases secretion of insulin
2. It promotes regeneration of islet cells.
3. It increases utilization of glucose: It is shown to increase the activities of enzymes responsible for utilization of glucose by insulin dependent pathways, an increase in phosphorylase activity, decrease in gluconeogenic enzymes and sorbitol dehydrogenase and
4. It causes inhibition of glucose absorption from intestine, the exact action being unknown. It could be involve one or more mechanisms

Uses
Gymnema has most important role in Ayurvedic medicine for centuries. Its use has been confined primarily to the management of diabetes mellitus and similar hypo/hyperglycemic condition.

2. Momordica charantia (Karela)[10, 11]
Family: Cucurbitaceae
Genus: *Momordica*
Species: *Charantia*
Parts are used- Fruits, seeds

Chemical constituents
- The main constituents of bitter melon which are responsible for the ant diabetic effects are triterpene (Momordicin, Charantin), steroid, alkaloid, inorganic, lipid, and phenolic compounds

Mechanism of Action[18]
Oral administration of fresh fruit juice (dose, 6 c.c. /kg. body wt.) lowered the blood sugar level in normal and alloxan diabetic rabbits. A p-Insulin, polypeptide from the fruits and seeds rapidly decreased and normalized the blood sugar level in rats. Studies have reported that the compounds are more effective than the oral hypoglycemic agent tolbutamide.

Uses
Apart from anti-diabetic property, Bitter melon is also traditionally known for its other medicinal properties such as anticancer, anti-inflammation, antivirus and cholesterol lowering effects.

3. Allium Sativum (Lahsun)[11, 12]
Synonyms: Garlic (Eng.), Lasan
Family: Amaryllidaceae
Subfamily: Allioideae
Genus: *Allium*
Species: S*ativum*
Parts used: Ripe Bulb

Chemical constituents
1. It contains a wealth of sulphur compounds most important for the taste is Allicin, which is produced enzymatically from allin.
2. It also contain 65% water, 28% carbohydrate, 2.3% organosulphur compound, 2% proteins, 1.2% free amino acid.

Mechanism of Action
In diabetic patients, it was reported that garlic oil can correct hyperglycemia. In addition, a precursor of various allyl sulfide constituents of garlic oil, S-allyl cysteine sulfoxide (allin), was shown to have a hypoglycemic effect similar to that of glibenclamide.

Garlic has been found to be effective in lowering serum glucose levels in STZ-induced as well as alloxan-induced diabetic rats and mice.

Most of the studies showed that garlic can reduce blood glucose levels in diabetic mice, rats and rabbits. It is clear how garlic actually works in alleviating hyperglycemia. The hypoglycemic is not action of garlic could possibly be due to an increase in pancreatic secretion of insulin from β-cells, release of bound insulin or enhancement of insulin sensitivity.

Uses
1. Antihelmentic, Anti-bacterial.
2. Antibiotic, Antioxidant, Antiseptic
3. Carminative, Cholagogue.
4. Anti-thrombolytic, Antihyperlipidimic
5. Angina pectoris

4. Ocimum sanctum Linn. (Tutsi)[13]
Family: Labiatae
Genus: Ocimum
Species: O. tenuiflorum

Chemical constituents-
Volatile Oil (eugenol and carvecrol)

Mechanism of Action
Ocimum sanctum exerts its anti-diabetic action probably by increasing the glucose uptake in to the cells.

Pharmacological Effect
Randomized, placebo-controlled, single bind, crossover trial studied the effects of *Ocimum sanctum* (dried leaf 2.5g daily) on fasting and postprandial blood glucose and serum cholesterol levels in patients diagnosed with non-insulin dependent diabetes mellitus. 40 patients, 20 of whom were receiving oral hypoglycemic drugs and twenty of whom were newly diagnosed without a *history* of anti diabetic drug use, took 2.5 g of Ocimum sanctum leaf or placebo in water on an empty stomach upon rising, followed by the other treatment for four weeks. Investigators were blinded to the sequence of treatments. The results showed that Ocimum sanctum treatment caused a significant decrease in both fasting and postprandial blood glucose levels compared with placebo. A mild reduction in total cholesterol levels was also observed. The mechanism responsible for the hypoglycemic activity of sacred basil is not known but Gymnema Sylvester raises levels of insulin.

Uses
Tutsi is reported to possess beneficial effect in cough, in gastro intestinal disorders and in inflammatory disorders. Antioxidant, anti-cataract activity, aeliorate the derangement in lipid metabolism in diabetics and antidiabetic.

***5. Trigonella foenum-graecum*[12, 13]**
Family: Fabaceae
Genus: *Trigonella*
Species: *foenum-graecum*
Parts used: seeds, leaves

Chemical constituents
Pyridine type alkaloid (trigonelline), steroidal saponin diosgenin and an non-essential amino acid (-4-hydroxy isoleucine).

Mechanism of Action
Clinical trials on people with type 2 diabetes show that fenugreek has the valuable property of reducing the rate at which sugar is absorbed from the stomach during the process of digestion; it also appears to be capable of stimulating the pancreatic cells to increase insulin production. Both these actions are believed to be a result of the action by an amino acid present in fenugreek called 4-hydroxyisoleucine.

Uses
Along with protection against hyperglycemia in patients with diabetes, numerous other reported beneficial effects of fenugreek are as an antioxidant, anticarcinogenic, anti-microbial, anti-ulcer, anti-obesity and hypocholesterolemic. Used in parathas and various Indian curries, *methi* has many health benefits. In recent times, clinical trials on people with type 2 diabetes show that fenugreek has the valuable property of reducing the rate at which sugar is absorbed from the stomach during the process of digestion; it also appears to be capable of stimulating the pancreatic cells to increase insulin production. Both these actions are believed to be a result of the action by an amino acid present in fenugreek called 4-hydroxyisoleucine.

***6. Tinospora cordifolia*[12, 13]**
Family: Menispermaceae
Genus: *Tinospora* Species: c*ordifolia*
Species: T. cordifolia
Parts used: Root

Chemical constituents
It contains different classes of chemical constituents such as alkaloids, diterpenoid lactones (Tinosporone, tinosporic acid) glycosides, steroids, sesquiterpenoid, phenolics, aliphatic compounds and polysaccharides.

Mechanism of Action
In blood glucose and brain lipids. Though the aqueous extract at a dose of 400 mg/kg could elicit significant anti-hyperglycemic effect in different animal models, its effect was equivalent to only one unit/kg of insulin. It is reported that the daily administration of either alcoholic or aqueous extract of T. Cordifolia decreases the blood glucose level and increases glucose tolerance in rodents. Aqueous extract also caused a reduction in blood sugar in alloxan induced hyperglycemia in rats and rabbits in the dose of 400 mg/kg. However, histological examination of pancreas has not revealed any evidence. Of regeneration of b-cells of islets of Langerhans and the possible mode of action of the plant is through glucose metabolism. The aqueous extract has also exhibited some inhibitory effect on adrenaline-induced hyperglycemia. Ethyl acetate extract of its roots has afforded a pyrrolidine derivative with hypoglycemic effect.

Uses
Other reported medicinal properties are hepatoprotective, anti-inflammatory, anti-oxidant, anti-allergic, immunomodulatory and anti-neoplastic activity.

***7. Jambul (Syzygium Cumini)*[12,18]**
Family: Myrtaceae.
Genus: *Syzygium*
Species: c*umini*
Parts used: fruits

Chemical constituents
Jambul seeds contain a glycoside, named Jamboline which helps in the maintenance of glucose levels as in the normal limits. The Jambul fruits also contains natural acids which helps in healthy secretion of digestive

enzymes. Thus, supports the liver system and the digestive system.

Mechanism of Action

It has significant decrease in the levels of blood glucose and increase glucose tolerance. The hypoglycemic efficacy was found to be comparable with that of glibenclamide, a standard hypoglycemic drug.

Uses

It cures many health problems like cardiac, diabetes, ulcer, diarrhea and liver. α-Amylase inhibition, anti inflammatory, reduce oxidative stress and β -cell regeneration.

8. Andrographis paniculata Nees.l **(Kalmegh)**[12,13,18]

Family: Acanthaceae
Genus: *Andrographis*
Species: *A. Paniculata*
Parts used: Whole plant
Chemical constituents:

Diterpene lactones (andrographolide, Kalmegh and neoandrographolid)

Mechanism of Action

A significant decrease in blood glucose levels was observed on glucose tolerance test as compared to the untreated group. The authors concluded that the drug inhibits glucose absorption in the intestine.

Uses

Kalmegh has been used for liver complaints and fever, and as an anti-inflammatory and immunostimulant. In clinical trials, Andrographis extract has been studied for use as an immunostimulant in upper respiratory tract infections and HIV infection. The potential of andrographolide as an anticancer agent is being investigated. However, clinical evidence to support the use of Kalmegh for any indication is lacking.

9. Zingiber officinale[18, 19,20]

Family: Zingiberaceae
Genus: *Zingiber*
Species: *Z. Officinale*

Common name: ginger
Parts used: Fresh ginger
Chemical constituents: Gingerols, shogaol

Mechanism of Action
Gingerol and Ginger, Zingiber officinale is commonly used as an ingredient in foods and medicine. Compelling data show that ginger extract has hypoglycemic, insulinotropic and sensitizer effects on healthy humans and on experimental animals. More recently, Liand colleagues reported that ginger extract enhanced insulin release and reduced insulin resistance. One clinical study reported that consumption of ginger powder, 3 g per day for 30 days, significantly reduced blood glucose and lipids in T2D patients. Conversely, another study stated that consumption of ginger powder, 4g daily for 3months, did not alter blood sugar and lipids in patients with coronary artery disease. This discrepancy may result from the variation in chemical composition of different ginger preparations. Gingerol and shogaol are the main active compounds in ginger extract. Gingerol was shown to attenuate sodium arsenite-induced T2D. This attenuation is related to islet-cell protection and increased insulin receptor signaling. The role of shogaol in T2D treatment is not clear although this compound showed an elevation of glucose uptake in response to insulin in muscle and adipose cell.

Uses
1. It has strong analgesic action
2. Its extract shows effect on blood pressure and heart rate.
3. Ginger is also having significant Hepatoprotective activity.
4. It has neuroprotective action.

10. *Camellia sinensis*[9,12,15,18]
Family: Theaceae
Genus: *Camellia*
Species: *C. Sinensis* Parts used: leaves
Chemical constituents
Caffeine and catechins.

Mechanism of Action[15]
Inhibits development of insulin resistance, hypoglycemia and other metabolic effects. also decreases glucose absorption from intestine.

Uses
1. Analgesic
2. Anticancer
3. Antispasmodic, Appetite Depressant, Astringent, Circulation
4. Nervine refrigerant
5. Stimulant

HERBAL ANTI-DIABETEC FORMULATION AVAILABLE AND BENEFITS
Helps to normalize blood sugar level controls and regulate weight, controls sugar craving reduces the taste of sugar when it is on the mouth curb sweet tooth for Cholesterol natural way to help control blood sugar.[20]

Advantages of Herbal Medicine
There are numerous advantages of herbal medicine. considering use of herbal medicine to treat health conditions should speak with a qualified health professional.

There are number of advantages associated with using herbal medicines as opposed to pharmaceutical products. Examples include the following:
Reduced risk of side effects: Most herbal medicines are well tolerated by the patient, with fewer unintended consequences than pharmaceutical drugs. Herbs typically have fewer side effects than traditional medicine, and may be safer to use over time.[21,22]

Effectives with chronic conditions: Herbal medicines tend to be more effective for long-standing health complaints that don't respond well to traditional medicine. One example is the herbs and alternative remedies used to treat arthritis. Vioxx, a well-known prescription drug used to treat arthritis, was recalled due to increased risk of cardiovascular complications. Alternative treatments for arthritis, on the other hand, have few side effects. Such treatments include dietary changes like adding simple herbs, eliminating vegetables from the nightshade family and reducing white sugar consumption.

Lower cost: Another advantage to herbal medicine is cost. Herbs cost much less than prescription medications. Research, testing and marketing add considerably to the cost of prescription medicines. Herbs tend to be inexpensive compared to drugs.

Widespread availability: Yet another advantage of herbal medicines are their availability. Herbs are available without a prescription.

SOME OTHER NEW PLANTS FOR ANTI-DIABETE POTENTIAL[16]

Botanical name	Family	Activity reported
Beta vulgaris L.	*Beta vulgaris L.*	*Increases glucose tolerance in OGTT*
Butea manosperma	Cesalpinaceae	Anti - hyperglycemic
Cynodon dactylon	*Poaceae*	*Anti-hyperglycemic*
Bombax ceiba L.	*Malvaceae*	*Hypoglycemic*
Glycyrrhiza uralensis	Papilionaceae	Decreases the blood glucose levels
Morus indica. L.	*Moracea*	*Hypoglycemic*
Nigella saliva	*Ranunculaceae*	*Hypoglycemic*
Morus inignis L.	*Moraceae*	*Hypoglycemic*
Murraya koenigii L.	*Rutaceae*	*Hypoglycemic, increases glycogenesis*
Ocimum gratissinuim	*Lamiaceae*	*Hypoglycemic*
Psacalium decompositum	*Asteraceae*	*Hypoglycemic*
Phyllanthus sellowianus.	*Euphorbiaceae*	*Hypoglycemic*
Urtica dioica	*Urticaceae*	*Hypoglycemic*

CONCLUSION

Literature survey of current topic suggests that a lot of work has been undertaken to establish the anti-diabetic potentials of several drugs, ranging from homeopathy and Ayurvedic to formulate. The herbs mentioned have proven to be promising in the treatment of diabetes and its complications in the near future. Therefore, there is a need of more well documented clinical trials and more laboratory work to isolate the active principles, their pharmacological actions and toxicity.

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