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ROLE OF HERBAL MEDICINES IN MANAGEMENT OF DIABETES: AN UPDATED OVERVIEW

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ABSTRACT

Introduction:

Diabetes is a serious metabolic complaint affecting millions of people today. The allopathic drugs used for treatment suffer numerous complications. Many herbal remedies can be used to treat diabetes. These herbs have no side effects and numerous drugs are deduced from the herbal sources. The purpose of this methodical review is to study diabetes and to epitomize the available herbal drugs with superiority over allopathic drugs for this complaint.

Methods:

The current review was structured by studying papers in the context of diabetes and effective herbal treatment from the databases, including Scopus, Wiley, Springer, Science Direct, and PubMed.

Results:

Diabetes is substantially caused due to a high quantum of reactive oxygen oxidative stress and an increase in reactive oxygen species that can have major goods. Herbal drugs contain a variety of natural antioxidants, similar to tannins, flavonoids, Vitamin C, and Vitamin E that can maintain β- cells performance and drop glucose situations in the blood.

Conclusion:

According to published results, it can be concluded that herbal drugs are more affordable and have lower side goods in comparison to synthetic medicines, and are more effective in the operation of diabetes.

Keywords: Diabetes, Types, Treatment, Herbal medicines, Role of herbal drugs

INTRODUCTION

Diabetes mellitus could be a cluster of metabolic conditions characterized by blights in hormone stashing, hormone action, or both. The habitual symptom of the polygenic complaint is related to long injury, dysfunction, and failure of colorful organs, particularly the eyes, kidneys, liver, heart, and blood vessels. The pathogenic process may vary from response destruction of the β-cells of the duct gland with resulting hormone deficiency to abnormalities that lead to resistance to hormone action. The abnormalities in sugar, fat, and macromolecule metabolism in polygenic disease are due to the deficient action of hormones on course tissues. Deficient hormone action results from inadequate hormone secretion or diminished tissue response to hormone **[1-3]**.

Defects in insulin secretion and defects in insulin action frequently coexist in the same patient, and it is often unclear which abnormality, if either alone, is the primary cause of hyperglycemia. Hyperglycemia is marked by symptoms of polyuria (increasing urine frequency), polydipsia (excess thirst), weight loss, sometimes polyphagia (excess hunger), and blurred vision. Acute, life-threatening consequences of uncontrolled diabetes are hyperglycemia with ketoacidosis or non-ketoacidosis hyperosmolar syndrome. Long-term complications of diabetes suffer from retinopathy with a potential loss of vision; nephropathy leading to renal failure; peripheral neuropathy with risk of foot ulcers, amputations, and Charcot joints **[1-3]**.

According to statistics, 2.8% of the world's population suffers from this disease and it is expected to increase to more than 5.4% by 2025. Diabetes is taken into account and can be treated easily by early diagnosis, treatment, and lifestyle changes. At the current time, different treatments, similar to insulin remedy, pharmacotherapy, and diet remedy, are prevailing to control diabetes. Several types of glucose-lowering medicines that ply anti-diabetic effects through different mechanisms are present. These mechanisms include enhancing insulin stashing by sulfonylurea and meglitinides medicines, rising supplemental immersion of glucose by biguanides and thiazolidinediones, and

delaying the immersion of carbohydrates from the intestine by nascence-glucosidase, and reduction of hepatic gluconeogenesis by some medicines. In the once three decades, despite the significant exploration made in the treatment of diabetes, the results of treatment in cases are still not perfect. These treatments have some disadvantages like medicine resistance (reduction of effectiveness), side goods, and toxins. For illustration, sulfonylureas lose their effectiveness after 6 years of treatment in 44 cases. It's also observed that the glucose-lowering drugs aren't suitable to control hyperlipidemia to the extent hence further addition of antihyperlipidemic is needed in remedy. In addition, the side effects of drugs and their relations with each other further may increase complications. At the moment the intelligence of the public is shifting further toward natural sources for diabetes. Major contents of natural or herbal drugs include carotenoids, flavonoids, terpenoids, alkaloids, glycosides, and antioxidants that exhibit anti-diabetic effects. The anti-hyperglycemic property of herbal medicines is frequently due to their capability to ameliorate the performance of pancreatic towels, which might be due to adding insulin concealment or reducing the intestinal immersion of glucose. The number of people with diabetes moment has been rising and causing enterprises in the medical community and the public. The main purpose of this composition is to introduce and suggest several effective herbal drugs or plants based remedy used for treating or managing diabetes **[2-4]**.

History - According to Egyptians Diabetes was first identified and measured by the symptoms of polyuria and weight loss. The greek physician “Aertaeus" has given the term Diabetes. Diabetes is called ‘Madhumeha’ by ancient Hindu physicians.

Types of Diabetes Mellitus: [1-4]

Type 1 Diabetes (Insulin-dependent).

Type 2 Diabetes (Non-insulin Dependent).

Cause -

Type 1 diabetes is an autoimmune disorder. It's believed that a combination of genetic predisposition and additional environmental factors provoke the immune system into attacking and killing the insulin-producing cells in the pancreas **[1-4]**.

Obesity is a leading cause of insulin resistance – about 90% of people with type 2 diabetes are overweight or obese. Genetic factors may be more likely involved in the cause of type 2 diabetes. Genetic history of the disease increases the risk of causing diabetes **[1-4]**.

Signs and symptoms:

Some common signs & symptoms associated with diabetes include excessive thirst, weight loss, fatigue, nausea, retarded wound healing, skin infections, hunger problems, etc. **[4]**.

MATERIALS & METHODS

The current review was structured by detailing the papers about diabetes and effective herbal treatment amongst the databases, including Scopus, Wiley, Springer, Science Direct, and PubMed as far as possible only the justified results were taken into consideration. The attempt was made to bring the most recent work performed in the reviewed area.

RESULTS & DISCUSSION

Why do we need Herbal Drugs? As currently available antidiabetic drugs are harmful and have critical side effects in various aspects. It's reported that over to72.8% of people with diabetes are switching to herbal drugs, salutary supplements, and other complimentary indispensable drug curatives. Some common examples of the currently available synthetic drug include: Pioglitazone associated with Liver toxicity and weight gain, Acarbose results in gastrointestinal disturbances, and Tolbutamide & Glyburide cause hypoglycemia & weight gain, Sitagliptin, Saxagliptin, & Linagliptin causes nasopharyngitis, headache, & nausea **[3-7]**.

Role of Herbal Drugs:

Medicinal plants constitute the natural wealth of the country. These medicinal plants provide primary health care services to the rural populations. According to ancient literature, more than 800 plants contain anti-diabetic properties. To date back, herbal formulations exist and are still widely consumed all over the world. In recent years, a prominent number of natural product-derived agents, such as lovastatin, pravastatin, and FK-506, have been discovered by employing mechanism-based screening approaches involving the cellular or biochemical targets. In their assay design, in addition, a large number of natural products, especially plant-derived drugs are continuously discovered based on traditional medical practices. It was estimated that nearly 80% of the world population depends on traditional herbal drugs for primary health care **[3-7]**.

Herbs or Plants Possessing Antidiabetic Effects:

Veritably High figures of medicinal shops are being used to treat diabetes and affiliated conditions. The recent NAPRALERT database shows 1300 species of plants representing further than 750 rubrics within 190 families, covering lower plants like algae and fungi to nearly all types of advanced plants. Numerous of these plants have been

used ethnopharmacologically in the operation of diabetes. Although numerous of these plants have been studied experimentally to validate their physiological exertion, chemical, and pharmacological parcels having the anti-diabetic effects are less well studied. A high number of potentially bio-active motes are insulated and linked, which include complex carbohydrates, alkaloids, glycopeptides, terpenoids, peptides, amines, steroids, flavonoids, lipids, coumarins, sulfur composites, and inorganic ions **[3-7]**.

Common herb-drug relations in diabetes:

The co-administration of antidiabetic herbs and pharmaceutical agents may affect in HDIs leading to enhanced effects (which may be desirable clinically), dropped pharmacological effects, or adverse medicine events, similar to hypoglycemia. The following section provides a brief discussion of common antidiabetic sauces and their implicit relations with antidiabetic agents. Literature quests were conducted with the standard databases to date.

Aloe vera: (*Aloe barbadensis*)

Aloe Vera belongs to the family Liliaceae, one of further than 400 species of the rubric Aloe. Carbohydrates and galacturonic acid are the major factors of Aloe. Traditional literature reveals a large range of clinical uses of this factory from cosmeceuticals to immunity and organ care. In diabetes, aloe vera shows a reduction in blood glucose situations **[4-7]**.

Karela—*Momordica charantia*

Momordica charantia, karela, or bitter melon. Several chemical ingredients are present in its juice, including sterols, glucoside fusions, and charantin polypeptides. Karela has been subordinated to expansive clinical studies in combination with common antidiabetics. High efficacity has been reported when used together with metformin, glymidine, and glibenclamide. In one clinical trial, 400 mg of chloroform/ benzene karela extract was combined with 50% of the full clinical doses of either metformin or glibenclamide in NIDDM cases. Results showed that the combined interventions inspired a lesser hypoglycemic effect when compared to that of full doses of metformin or glibenclaminde alone, indicating a possible cumulative effect. Analogous results have also been attained in beast studies whereby combined treatments of karela fruit juice/extract and metformin have been shown to produce a lesser hypoglycemic effect than either treatment alone in rat models of diabetes **[4-7]**.

Ginger—*Zingiber Officinale*:

Ginger is generally used as a spice as well as a drug numerous times. Crude ginger contains nearly 9 percent lipids or glycolipids

and 5 – 8 percent oleoresin. The pungent principles, which account for 25 percent of the oleoresins, correspond substantially to gingerols and related phenolic composites. The aqueous extract is antidiabetic in numerous countries. It's assumed that the antidiabetic effect of ginger is due to antioxidant and anti-glycation properties, and its capability to express the glucose transporter Glut 4. In a study in a rat model of streptozotocin (STZ) convinced diabetes, concurrent treatment of ginger extract (25 or 50 mg/ kg) and glibenclamide (5 mg/ kg) significantly dropped non-fasting blood glucose situations by 26 and 25%, independently, compared to7.9 % reduction when only glibenclamide was used **[4-7]**.

***Azadirachta indica*: (Neem)**

Neem is a tropical plant that's native to India and Asia. Every part of the plant is full of antiseptic and medicinal properties. Neem has been an integral part of Indian and Chinese drugs since ancient times. Nearly all corridors of the neem tree- leaves, flowers, seeds, fruits, roots, and dinghy have been consumed traditionally for a variety of treatments. Some Clinical studies have suggested that some composites of Azadirachta indica (Neem) could be useful in diabetes mellitus in controlling blood sugar. Alcoholic extract from neem reported anti-hyperglycemic activity in streptozotocin-treated rats and this effect is because of the increase in glucose uptake and glycogen deposit in insulated rat hemidiaphragm **[7-11]**.

***Eugenia jambolana*: (Indian gooseberry/ Jamun)**

Jamun (Eugenia jambolana) is used as one of the common remedies for diabetes. The aqueous extract, alcoholic extract, and lyophilized powder exhibited a reduction in blood glucose position. The extract of Eugenia jambolana pulp displayed a hypoglycemic effect in streptozotocin convinced diabetic mice within 30 min of administration, whereas the seed of the jambolana fruit took 24 hrs. The oral administration of the extract showed an acceptable rise in serum insulin situations in diabetic rats **[7-11]**.

***Ocimum sanctum*: (holy basil)**

It's notorious by the name tulsi. Since ancient times, this plant is known for its medicinal property. Holy basil is a relative of the further familiar species used in cooking known to the ayurvedic medical tradition as tulsi, it has been called the" Queen of Sauces" since the times of ancient civilization in India. The aqueous extract of leaves of *Ocimum sanctum* redounded in the significant reduction in blood sugar position

in both normal as well as alloxan convinced diabetic rats. Oral administration of the aqueous extract (200 mg/ kg) for 30 days results in a drop in the tube glucose position by roughly 9.06 and 26.4% on 15 and 30 days of the trial independently. Renal glycogen content raised by 10 fold while cadaverous muscle and hepatic glycogen situations were reduced by 68 and 75% independently, in diabetic rats, compared to control.

[12].

***Tinospora cordifolia*: (Guduchi)**

Guduchi is a large, rough, evanescent climbing shrub. A largely potent condiment used in Ayurveda for the operation of diabetes and keeps the function of various organs in harmony, belonging to the family Menispermaceae. It's abundantly planted throughout India and is generally known as Guduchi. Oral administration of the extract of Tinospora cordifolia (T.cordifolia) roots for 6 weeks displayed a significant reduction in blood and urine glucose and lipids in serum in alloxan convinced diabetic rats. The extract also defended a drop in body weight **[13]**.

Cinnamon

It is a fragrant spice obtained from the bark of a tree *Cinnamonum Zylanicum*. It is a popular ingredient in food preparations. A study found in humans that cinnamon may improve levels of glucose, insulin and insulin sensitivity, lipids, or fats, in the blood, it also acts as an antioxidant another study suggested that taking a cinnamon supplement might lead to lower fasting blood glucose levels less total cholesterol and "bad" low-density lipoprotein cholesterol higher levels of "good" high-density lipoprotein cholesterol reduction in triglycerides, or fat, in the blood increased insulin sensitivity **[14]**.

Curry leaves (*Murraya koenigii*)

It controls diabetes so is one of the important home remedies for diabetes. Hereditary diabetic patients also get the best benefit from its intake. Chewing (8-10) curry leaves on an empty stomach is very effective for bringing sugar levels in urine and blood to normal **[15-18]**.

***Allium-cepa:* (Onion)**

Various ether soluble fractions, as well as insoluble fractions of dried onion powder, showed anti-hyperglycemic activity in diabetic rabbits. Administration of a sulfur-containing amino acid from *Allium cepa*, S-methyl cysteine sulphoxide (SMCS) (200 mg/kg for 45 days) to alloxan convinced diabetic rats significantly controlled blood glucose as well as lipids in serum and tissues with normalization of the activities of liver hexokinase, glucose 6-phosphatase, and

HMG Co-A reductase. When diabetic patients were given a single oral dose of 50 g of onion juice, it significantly controlled post-pardinal glucose levels **[16-18]**.

Green tea (*Camellia sinensis*) consumption has been used traditionally to control blood sugar in the body. It is associated with the prevention of type 2 diabetes, lowering fasting blood levels of glucose, reducing triglyceride and free fatty acids, and enhancing the ability of adipocytes to respond to insulin and absorb blood sugar. Its consumption also increases the body's ability to utilize blood sugar. Green tea polyphenols regulate the expression of genes involved in glucose uptake and insulin signaling **[16-18]**.

Gurmar (*Gymnema sylvestre*)

This plant contains gymnemic acid as a chief constituent effective against obesity which probably slows down the glucose absorption in the blood. Gymnema Sylvester also helps in the excretion of cholesterol through feces **[16-18]**.

Ispaghula husk (*Plantago ovata*) is naturally safe for the treatment of diabetes; the main effect is on reducing constipation thereby supporting the reduction of glucose levels **[16-18]**.

Leucas-lavandulifolia:

The plant of Leucas lavandulifolia Sm. of family Labiatae has been estimated for its antidiabetic exertion in alloxan convinced diabetic rats as well as for its in vitro antioxidant property. It was observed that methanolic extract of *L. lavandulifolia* displayed significant antidiabetic effects in dose dependant manner, but the effect was not more promising than glibenclamide **[19]**.

Shilajit :

Shilajit is a herbal medicine that is used in diabetes to improve the lipid profile & lower blood glucose levels, it is an herbal booster for the overall health of the body. Shilajit is the safest herbal drug for the long-term treatment of diabetes but not for heart patients, in a hypertensive patient, it induces blood pressure **[20]**.

Fenugreek:

Fenugreek is an annual herb that belongs to the Leguminosae family. The leaves, as well as seeds, are used as an antidiabetic herb. It is a rich source of proteins, vitamins, and minerals. Fenugreek purifies the blood & regulates the lipid profile which exhibits the antidiabetic Property. Administration of fenugreek increases glucose metabolism & normalizes kinase activity **[20]**.

Black Seeds:

Black seeds are taken in the whole form or in the form of the cold-pressed oil that is extracted from the seeds. The most important property is the use of black seed or black

seed oil for regulating blood sugar levels in diabetics. The oil may be especially beneficial for Type-2 diabetics as it can benefit them in multiple ways primarily due to its antioxidant properties. The powerful antioxidant property of black seeds or *kalonji* has a positive impact in several ways on the overall health of Type-2 diabetics **[24]**.

Rauwolfia serpentina:

Commonly known as 'snakeroot', is an important medicinal plant familiar to the Indian subcontinent and South-East Asian countries. The plant contains therapeutically important indole alkaloids. It has also been reported that extracts of the roots from R. serpentina possess hypoglycemic and hypolipidemic activity in animal models. Based on the data, we hypothesize that extracts of Rauwolfia serpentina may contain molecules that are active against diabetes and its related complications, primarily through aldose reductase inhibition **[26-31]**.

Acacia Arabica:

The animal study was conducted in King Fahd Research Center, King Abdulaziz University Jeddah Kingdom of Saudi Arabia from December 2012 to January 2013. Thirty-six female albino rats were divided into 2 equal groups; the first group was the control, and the second was the streptozotocin-induced diabetic group. Each group was further divided into 3 subgroups, each of 6 rats; the first was left untreated, and the second and the third were treated with Acacia Arabica extract orally for 21 days (100 mg/kg and 200 mg/kg for the second and third group respectively). On the 21st day, blood samples were taken through the retro-orbital plexus of overnight fasted rats under ether as an anesthetic for determination of serum glucose, insulin,), triglycerides (TG), total cholesterol (TC low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), malondialdehyde (MDA), and coenzyme Q10 (Co-Q10). It was found that there was a significant decrease in levels of insulin resistance, serum glucose, TC, TG, LDL-C, and MDA, and a significant rise in HDL-C and Co-Q10 was observed in the treated diabetic groups when matched to the untreated diabetic group. Acacia Arabica extract was having hypoglycemic, hypolipidemic, and antioxidant properties, therefore, it can be further studied for the treatment of diabetes in humans **[30-33]**.

Phyllanthus amarus:

Phyllanthus amarus is a medicinal plant that is used substantially in central and southern India as a Hypoglycemic Factor. Oral administration of an extract from the leaves

(400 mg/ kg/ BW) for 6 weeks caused a significant reduction in blood glucose situations in alloxan-convinced diabetic mice and led to a significant enhancement in the weight of diabetic mice. Also, there was a reduction in Robison Ester and fructose 1, 6-diphosphatase conditioning in the liver. The glucokinase exertion, in comparison with the control group, rises during treatment in the liver of the diabetic rats **[30-33]**.

Eucalyptus Camaldulensis:

The study was based on the determination of the composition of the essential oil of *Eucalyptus camaldulensis* leaves and the evaluation of its *in vitro* antioxidant and antidiabetic properties. The composition of the essential oil from *Eucalyptus camaldulensis* leaves was analyzed by Mass Spectrometric detection around 29 compounds representing 99.10% of the total oil were identified. The components of the oil were *p*-cymene, 8-cineole, 1-(S)-α-pinene, and R-(+)- limonene. The antidiabetic effects of the essential oil were evaluated using inhibition of 2,2-diphenyl-1-picrylhydrazyl, hydroxyl, and superoxide radicals, inhibition of hydrogen peroxide, and lipid peroxidase assays **[30-33]**.

Table 1: Herb–antidiabetic drug co-administration studies [33]

Herb	Co-administered Anti-Diabetic Drug	Findings
Aloe-vera	Glibenclamide	Improved effect on lowering the blood glucose.
Bitter Melon	Metformin	A decrease in serum glucose was found in the combination with fruit juice extract at half the normal dose of metformin.
Ginger	Glibenclamide	The Synergistic effect with ginger extract reduces blood glucose levels greater than glibenclamide as single
Sesame oil	Glibenclamide	Improved anti-hyperglycemic effect in combination
Garlic	Metformin	garlic is capable of affecting the pharmacokinetics of Metformin resulting in decreased blood glucose level

CONCLUSION

All over the world, herbal medications are being helpful and widely used for the treatment of diabetes. Herbs are used to manage various types of diabetes and their complications. Various medicinal plants have been considered for their probable hypoglycemic actions and the researchers have carried out some preliminary investigations. Scientific authentication of several Indian plant species has proved the efficacy of the botanicals in reducing the sugar level could be considered of possible therapeutic value. Thus, many different plants have been used individually or in formulations for the treatment of diabetes. Interactions of antidiabetic drugs and herbs may result in antagonistic or enhancement effects. The enhancement of glucose-lowering has the possibility of causing hypoglycemia, hence monitoring of potential adverse effects is required and hence it is

when combining the two compounds. Despite the potential for adverse effects, the combination of these herbs and antidiabetic medications has been more commonly shown to have positive clinical implications as it could lead to enhanced antidiabetic effects, potentially enabling a reduction in the dose of antidiabetic agents, thereby minimizing their side effects. Herbal medicines might be a promising therapy in the management of diabetes.

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CONFLICT OF INTEREST:

None

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