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AN ORGANISED ANALYSIS OF HERBAL MEDICINE FOR TREATMENT OF DIABETES MELLITUS: AN SYSTEMATIC REVIEW

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ABSRACT
Diabetes mellitus is an increasingly prevalent metabolic disorder that poses a serious threat to global public health. It arises from the deficiency or ineffective production of insulin by the pancreas, leading to fluctuations in blood glucose levels. Although various chemical agents exist to manage the condition, a complete cure has yet to be found. Extensive research has uncovered numerous traditional medicines, particularly those derived from plants, that exhibit hypoglycemic properties. The World Health Organization (WHO) has identified over 21,000 medicinal plants used worldwide, many of which have proven antidiabetic effects. This review compiles evidence on various herbal and polyherbal formulations traditionally employed to manage diabetes mellitus, highlighting their therapeutic potential and the importance of further exploration in this area. By examining these natural remedies, we aim to enhance understanding of their role in controlling blood glucose levels and mitigating complications associated with diabetes.

KEYWORDS: Diabetes mellitus, Plant, Herbal, Traditional Medicine, Polyherbal.

INTRODUCTION

Diabetes mellitus is a systemic metabolic disease marked by insufficient insulin secretion or action, persistent hyperglycemia, and abnormalities in the metabolism of proteins, fats, and carbohydrates. Serious side effects from this illness can include macrovascular disorders including coronary heart disease and peripheral vascular disease as well as microvascular problems like retinopathy and nephropathy.[1] Insulin and a variety of oral antidiabetic medications, such as glinides, biguanides, glucosidase inhibitors, and sulfonylureas, are currently available as therapy alternatives. However, these medicines are frequently expensive and difficult to obtain in developing nations.[2] Over 61 million cases of diabetes have been detected in India, dubbed the "diabetes capital of the world," and estimates suggest that figure could increase dramatically over the next several years. The rising incidence of diabetes emphasises how urgently alternative therapeutic modalities—especially those with roots in traditional medicine—are needed. For ages, a variety of medicinal plants—known as Rasayana in Indian traditional health systems—have been used to treat diabetes.[3] In order to address diabetes mellitus, a disorder that has significant financial and health costs worldwide, this review focusses on the potential of herbal medication preparations and plants that may offer efficient therapeutic solutions.[4] According to the International Diabetes Federation, 415 million people worldwide have diabetes, and by 2040, that number is predicted to rise to 642 million. Sedentary lifestyles, bad eating habits, and socioeconomic factors are among of the factors causing the incidence to rise; rates are much higher in urban areas than in rural ones. The necessity for focused educational interventions is further highlighted by research showing that those with lower levels of education are more likely to develop diabetes.[5] It is imperative to investigate and incorporate traditional medical methods with contemporary treatment regimens in light of the growing diabetes epidemic. Examining the effectiveness of different herbal remedies in the management of diabetes is the goal of this review, which may provide long-term solutions in areas where access to traditional medications may be limited.[6]

Diagnosis of Diabetes Mellitus

Blood sugar levels can be used to diagnose diabetes mellitus. Blood sugar levels in a healthy person should be less than 140 mg/dl (7.8 mmol/L) in the postprandial period, which occurs two hours after eating, and between 70 and 99 mg/dl (3.9 and 5.5 mmol/L) during fasting.

In a lab setting, the many tests performed to diagnose diabetes are as follows:

- Diabetes is indicated by a fasting blood sugar (FBS)* level of 126 mg/dl (7.0 mmol/L) or above.

- Two hours after eating, a postprandial blood sugar level of 200 mg/dl (11.1 mmol/L) or greater indicates diabetes.
- Oral Glucose Tolerance Test (OGTT)*: The patient takes a glucose solution after fasting, and diabetes is diagnosed if, after two hours, the blood sugar level is 200 mg/dl (11.1 mmol/L) or above.
- Glycated Haemoglobin (HbA1c)*: Diabetes is diagnosed when the HbA1c level is 6.5% or more.

Furthermore, although a finger prick blood sugar test is usually used for monitoring purposes rather than diagnosis, it can offer a rapid evaluation.[7]

Pathology

Oxidative stress plays a major part in the pathogenesis of diabetes mellitus. An imbalance between the generation of reactive oxygen species (ROS) and the ability of enzymatic or non-enzymatic antioxidants causes this disease. Free radicals like superoxide, hydroxyl radicals, and peroxyl radicals, as well as non-radical species like hydrogen peroxide, are examples of reactive oxygen species. Vitamins A, C, and E, carotenoids, glutathione, superoxide dismutase, glutathione reductase, and trace elements are examples of antioxidants. When ROS are present, low-density lipoprotein (LDL) cholesterol is oxidised. This is subsequently absorbed by macrophages' scavenger receptors, resulting in the development of foam cells and atherosclerotic plaques. These ROS have the ability to activate a number of harmful pathways that greatly accelerate the development of diabetes. The sorbitol aldose reductase route, the glucosamine pathway, electron transport chain failure, and protein kinase C activation are significant mechanisms impacted by oxidative stress. Amylin buildup, lipid peroxidation, atherosclerosis, amylin accumulation, programmed cell death, and impaired pancreatic beta-cell function can all result from stimulating these pathways. Nuclear factor erythroid 2-related factor 2 (Nrf2), a sequence-specific DNA binding factor, and its negative regulator, Kelch-like ECH-associated protein 1 (Keap1), have been found to play a significant protective effect against oxidative stress.[8]

IMPORTANT MEDICINAL PLANT HAVING DAIBETIC POTENCIAL

Bauhinia forficate

In Brazil, Bauhinia forficata, popularly known as pata de vaca (cow's hoof), is the most widely used herbal treatment for diabetes.[9] The genus Bauhinia belongs to the Caesalpiniaceae family, and its fresh leaves are the essential part of this plant that has hypoglycemic activity.[10] The antidiabetic effectiveness of Bauhinia forficata in diabetic patients was initially reported by Juliani (1941)[11] and Juliani (1931).[12] According to M.T. Pepato et al. (2002), a decoction of Bauhinia forficate was prepared by boiling 150 g of fresh leaves in 1 litre of water for 5 minutes, allowing the mixture to rest for 30 minutes, and then straining the liquid. The experiment's rats were housed in a 12:12 light-dark cycle at 22–25°C and fed a typical laboratory chow diet that was composed of 16% protein, 66% carbs, and 8% fat (wt./wt.). Two sets of rats—one with diabetes and the other without—were used in this experiment. After three days of administering 40 mg/kg body weight of streptozotocin (STZ) to the diabetic group, elevated blood and urine glucose levels were noted. A control group was then given drinking water, while another group was given Bauhinia for al decoction. The diabetic group receiving decoction demonstrated a significant reduction in both plasma and urine glucose levels after a 31-day course of therapy. In order to determine the exact mechanism of action of the decoction of Bauhinia forficata leaves and to discover any active substances, more research in the domains of pharmacology, biochemistry, histology, and chemistry is necessary. Type 2 diabetes should also be the subject of such research.[13]

Figure 1: Bauhinia forficate plant.

Gymnema sylvestre

The leaves of the plant Gymnema sylvestre (Asclepiadaceae) are used to manufacture herbal remedies. It is being investigated as a potential diabetic treatment. The herb gymnemate, sometimes referred to as "sweet urine," is utilised as a home treatment for diabetes in India and other Asian countries. The potential of gymnema leaves to lower blood sugar, or hypoglycemia, was first documented in the late 1920s.[14] Gymnema sylvestre crude extracts and their separated component dihydroxy gymnemic triacetate show a dose- and time-dependent hypoglycemic impact in streptozotocin-induced diabetic rats.[15] The ability of gymnemic acids to delay the blood's absorption of glucose caused the hypoglycemic effect. Gymnemic acid molecules' receptor placement in the intestinal absorptive outer layers is what causes low blood sugar. This stops sugar molecules from being absorbed in the intestine.[16] Furthermore, the glucose levels decrease due to the presence of dihydroxy gymnemic triacetate in the crude extract. By promoting the regeneration process and reviving the remaining beta cells, this enables the release of insulin.[17,18,19] Furthermore, it was demonstrated by Liu et al. (2009) that Gymnema sylvestre's aqueous leaf extract (OSA) stimulates insulin secretion from isolated

human islets and mouse cells in vitro without jeopardising the cells' ability to survive.[20] Normal rats' insulin and plasma glucose levels were unaffected by dihydroxy gymnemic triacetate, indicating that the novel chemical had a normoglycemic effect. The usual weight loss associated with STZ-induced diabetes is due to increased muscular wasting in diabetes.[21] The new chemical dihydroxy gymnemic triacetate, which was isolated from Gymnema sylvestre leaves, is a strong contender for use in complementary and alternative medicine to treat diabetes mellitus, according to a comprehensive review of the literature. This is due to the fact that the substance had favourable effects on the blood glucose levels and associated biochemical parameters of rats that were administered STZ to create diabetes.

Figure 2: Gymnema sylvestre plant.

Ricinus communis

Ricinus communis was a traditional Chinese medicine used to treat diabetes mellitus. It is also referred to as castor oil and is called Arandi in Hindi, Erandah in Sanskrit, and Amudam in Telugu. It belongs to the Euphorbiaceous family and was cultivated all over India for its seed oil. According to Susruta and Ayurveda, castor oil has been used in Greek and Egyptian traditional medicine from the sixth century B.C.[22] In Indian medicine, the plant's leaves, roots, and seed oil have been used to treat inflammation and liver disorders.[23] 50% of the ethanolic extract of this plant's roots, stem, and leaves showed antihyperglycemic activity in diabetic rats and a hypoglycemic impact in normal mice in early screening trials.[24] Although the blood glucose levels of the control animals in 1886 did not dramatically alter, the diabetic rats' blood glucose levels did significantly drop when the ethanolic extract was given to them over an extended period of time. The 50% ethanolic root extracts of Ricinus communis exhibited a dose-dependent effect on the blood glucose levels of diabetic rats up to a dosage of 500 mg/kg body weight. The largest decline in blood glucose was observed in the eighth hour, and higher dosages up to 2000 mg/kg body weight did not show any dose-dependent effects. A significant hypoglycemic effect was seen at 500 mg/kg body weight of 50% ethanolic extract, causing blood glucose levels to decline from 371 ± 21 mg/dl to 166 ± 19. Only one fraction (R18) effectively lowered the blood glucose levels of diabetic rats when twenty column-purified fractions of 50% ethanolic root extracts were tested for antihyperglycemic efficacy. Fraction R18 reduced the blood glucose from 379 ± 72 mg/dl at the start of the experiment to 294 ± 60 (a decrease of 22.4%), 284 ± 36 (25%), 184± 23 mg/dl (a decrease of 51.4%), 182 ± 40 mg/dl (a decrease of 51.9%), and 149 ± 11 mg/dl (a decrease of 60.6%) at the first, second, fourth, sixth, and eighth hours, respectively.[25] Both normal and alloxan-diabetic mice's blood glucose levels were found to be significantly lowered by the plant. A dose of 500 mg/kg body weight was found to be efficacious for Ricinus communis. The diabetic rats' body weight and lipid profile improved, and their blood glucose levels were considerably lowered to almost normal after receiving this ethanolic extract for 20 days. Additionally, the levels of insulin increased. The exact mechanism of action of the Ricinus communis root extract has to be clarified by more extensive pharmacological investigation, but it seems to have promise for developing an effective phytomedicine for diabetes.

Figure 3: Ricinus communis plant.

Swertia punicea

Swertia herbs are most frequently used as a traditional diabetes treatment.[26] The entire Swertia Punicea plant (5.6 kg) was extracted using 90% ethanol at room temperature to provide 940 g of crude extract. Next, petroleum ether, EtOAc, and n-butanol were applied one after the other to this crude extract. It belongs to the Gentianaceae family. The primary class of compounds found in this species, xanthonoids, and a few plant extracts have been reported to have notable hypoglycemic effects.[27] Mice with diabetes induced by alloxan show good hypoglycemic effectiveness when treated with the plant Swertia Punicea.[28] And, according to studies by Pen and Fang (2003), can reduce oxidative damage in diabetic mice.[29] Additionally, Swertia Punicea's ethanol extracts and ethyl acetate soluble fraction showed hypoglycemic effects in STZ-induced type-2 diabetic mice and may aid in reducing insulin resistance (IR).[30] The hypoglycemic activity of this plant is attributed to two important components: bellidifolin and methylswertianin. The 90% ethanolic extract of Swertia Punicea was administered to rats in the diabetic and control groups. After a 28-day course of treatment, the fasting blood glucose levels of both groups were assessed. The fasting blood glucose level of the diabetes control group was noticeably greater than that of

the normal control groups. The two doses of bellidifolin and methylswertianin, two of the plant's key components, dramatically reduced fasting blood glucose levels after one week of administration, and the levels stabilised after four weeks. Bellidifolin and methylswertianin at 200 mg/kg body weight/day shown stronger antidiabetic effects after four weeks of oral administration (significant reductions of 44.04% and 44.48%, respectively) than those at 100 mg/kg body weight/day (reductions of 37.99% and 38.93%, respectively).[31] Previous investigations have shown that the ethanol extract and ethyl acetate fraction of Swertia Punicea have strong anti-diabetic effects. Current studies show that xanthone derivatives, including methylswertianin and bellidifolin, have significant anti-diabetic effects in addition to their potential mechanism or mechanisms of action in mice with type-2 diabetes brought on by STZ. The mechanism of action of Swertia Punicea's hypoglycemic effect was found to be the reduction of insulin resistance. As a result, the herbal remedy Swertia Punicea helps treat type-2 diabetes mellitus and encourages the development of new phytomedicines for the condition. This could lead to the identification of more advantageous Swertia species for the treatment of type-2 diabetes.

Figure 4: Swertia punicea Plant.

Combretum Micranthum

Combretum Micranthum is a medicinal herb used to treat diabetes in Northwestern Nigeria. It belongs to the Combretaceae family and is well known in Hausa as "geza." This popular ethnomedical herb is used to treat a number of ailments in West Africa.[32,33] Approximately 80% of Nigerians treat their illnesses using natural treatments.[34] The herb has also been demonstrated to have antioxidant, antimicrobial, and anti-inflammatory properties.[35,36] The aqueous extract of Combretum Micranthum was prepared using a Soxhlet extractor. After that, it was dried at 45°C in an evaporator and stored at 4°C until it was time to utilise it. The hypoglycemic effect of this plant extract was assessed using the glucose tolerance test and normal rats' fasting blood sugar levels. The antihyperglycemic properties of this herb were tested in two animal groups: one with diabetes and the other without. The two groups received 100 mg/kg, 200 mg/kg, and 400 mg/kg body weight of the Combretum leaf extract in water1887 Micranthum, which was dissolved in normal saline (N/S); however, the optimal dosage of the extract was found to be 100 mg/kg. In contrast to the maximum decreases of 21.9% and 18.9% attained by 200 mg and 400 mg/kg body weight, respectively, the 100 mg/kg body weight dose of aqueous leaf extract considerably decreased the blood glucose level, with a maximum reduction of 24.6%.[37] In this plant study, it was shown that the aqueous leaf extract of Combretum Micranthum had promising antidiabetic activities for both type 1 and type 2 diabetes mellitus. Therefore, further investigation is needed to determine which active components are responsible for these traits.

Figure 5: Combretum Micranthum plant.

Sarcopoterium spinosum

Sarcopoterium spinosum species, a typical Mediterranean medicinal plant, is often used as an antidiabetic by Bedouin healers. Ethnobotanical surveys indicate that this plant is used in traditional Arab and Bedouin medicine to alleviate discomfort, diabetes, cancer, and digestive problems. Thorny burnet (syn: Poterium spinosum L.; Hebrew: "sira kotsanit," Arabic: "natsh" or "bilan") is another name for it.[38,39] This common and unique species can be found in Batha and the semi-steppe shrublands (phrygana) in the Eastern Mediterranean region. Sarcopoterium spinosum is a chamaephyte that is a member of the Rosaceae family.[40] The plant's root extract was the most effective at a dosage of 0.01 mg/ml when compared to lower or higher doses. The aqueous root extract was thought to have an antidiabetic effect on the rising hyperglycemia in the genetically diabetic mice.[41] Consequently, the aqueous root extract of Sarcopoterium spinosum increases insulin secretion in vitro, enhances glucose tolerance in vivo, and has insulin-like actions in target tissues. These results lend support to the traditional use of herbal medicine. Blood sugar levels can be lowered by Sarcopoterium spinosum.[42] The extract encourages myotubes, adipocytes, and hepatocytes to absorb glucose. The extract from Sarcopoterium spinosum also increases GSK3 phosphorylation in myotubes. The identification of active components in Sarcopoterium spinosum plant extract may provide the foundation for the development and improvement of new anti-diabetic medications.[43]

Figure 6: Sarcopoterium spinosum plant.

CONCLUSION

Diabetes mellitus is a widespread endocrine disorder affecting over 300 million people worldwide, representing a significant economic burden that can impede national development. Conventional allopathic therapies often have limited efficacy, carry risks of adverse effects, and can be prohibitively expensive, especially in developing countries. This scenario highlights the urgent need for innovative treatment strategies. In this review, we have compiled a list of hypoglycemic plants from India and abroad, showcasing their potential as effective alternatives in managing diabetes. These plant-derived compounds are not only more accessible but also free from the complexities of pharmaceutical synthesis. Isolating and identifying active constituents, along with establishing standardized dosages, can significantly enhance their therapeutic efficacy. Moreover, uncontrolled diabetes leads to severe complications, Including blindness, heart failure, and renal failure, further emphasizing the necessity for continued research into new hypoglycemic agents. By advancing our understanding of these natural treatments, we can develop evidence-based alternative medicines that improve health outcomes for individuals affected by diabetes mellitus. This approach promises to mitigate the impact of this condition and promote better overall well-being.

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