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A REVIEW ON INSIGHTS OF HERBAL ANTI-DIABETEIC AGENTS

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Abstract: Diabetes mellitus, a metabolic disorder characterized by inadequate insulin production or utilization, has become a global health concern. In this context, type 2 diabetes affects around 12% of urban India's population, making it a significant public health challenge. Suboptimal glycemic control, often due to poor adherence to conventional medications and associated side effects, underscores the need for alternative approaches. Herbal remedies are gaining attention for their perceived efficacy and lower risk of adverse effects.

The focus then shifts to the role of herbal drugs in diabetes treatment, emphasizing their advantages, including easy availability, minimal side effects, and cost-effectiveness. Ethnobotanical data reveal numerous plants with potential antidiabetic properties, showcasing examples such as Allium sativum, Artemisia pallens, Azadirachta indica, Bauhinia forficata, Eucalyptus globules, Gymnema sylvestre, Hibiscus rosa-sinensis, Ipomoea batatas, Ricinus communis, and Trigonella foenum. Each plant's hypoglycemic effects are detailed, providing insights into their mechanisms of action.

Despite significant strides in synthetic medicinal chemistry, herbal medicine remains a preferred healthcare option in many regions, driven by affordability and perceived safety. This review underscores the importance of careful consideration and monitoring when integrating plant-derived remedies into diabetes care, emphasizing the need for comprehensive and individualized approaches. The presented information contributes to the growing body of knowledge on herbal drugs, providing valuable insights for researchers, healthcare professionals, and individuals seeking alternative avenues for diabetes management.

Keywords
Diabetes mellitus, Insulin, Herbal medicines, Hypoglycemia

I. INTRODUCTION

Diabetes is a metabolic condition in which the body fails to produce or effectively use insulin, a crucial hormone for converting sugar and starches into energy. It results in persistent elevated blood glucose levels, defining diabetes mellitus. The human body tightly regulates blood glucose levels through insulin and glucagon. Glucagon's role involves releasing glucose from the liver into the bloodstream, allowing it to be transported to body tissues and cells for energy production [1].

Approximately 12% of urban India's population is affected by type 2 diabetes, making it the country with the highest number of such patients globally [2]. The suboptimal glycemic control rate is attributed to factors like insufficient adherence to oral antidiabetic drugs with frequent dosages and the occurrence of side effects, including hypoglycemia. Studies indicate that type 2 diabetes patients, transitioning from multi-dose to once-daily formulations, exhibit a 23% improvement in medication adherence, leading to reduced HbA1c levels [3].

The increasing concern over side effects linked to oral hypoglycemic agents has sparked a rising interest in herbal remedies for diabetes mellitus treatment. Traditional herbal medicines derived from plants are gaining prominence due to their perceived efficacy and lower risk of adverse effects. These herbal alternatives play a crucial role in the management of diabetes, offering a natural and potentially safer approach to addressing the condition. As a result, there is a growing inclination towards incorporating these plant-based remedies into diabetes care, reflecting a shift towards holistic and nature-based therapeutic options in the management of this medical condition [4].

Herbal or plant-based products contain abundant phenolic compounds, flavonoids, terpenoids, coumarins, and other constituents known for lowering blood glucose levels. Numerous herbal species have been documented in scientific and popular literature for their reported antidiabetic properties. Herbal drugs are recommended for their perceived effectiveness, minimal observed side effects in clinical practice, and cost-effectiveness. Traditional usage of medicinal and herbal plant products for treating diabetes mellitus has been prevalent across various countries for an extended period. This historical reliance underscores the enduring and widespread acknowledgment of their therapeutic value in managing diabetes [4, 5].

II. CLASSIFICATION OF DIABETES

- **Type 1 Diabetes Mellitus**

Type 1 diabetes results from the destruction of pancreatic beta cells responsible for insulin production, often due to T-cell mediated autoimmune disorders. It predominantly affects North America and Europe, constituting 10% of cases. Insulin remains the only treatment, with no preventive measures available. Primarily found in children, its termed juvenile diabetes. Regular monitoring, disciplined care, and awareness help manage blood glucose levels, ideally ranging from 80-120 mg/dl. Elevated levels may lead to frequent urination and dehydration, while very high levels can cause life-threatening ketoacidosis. Proper attention is crucial for managing potential complications, including seizures and unconscious episodes [6].

- **Type 2 Diabetes Mellitus**

Type 2 diabetes, also termed Non-Insulin Dependent Diabetes Mellitus (NIDDM) or adult-onset diabetes, is the most prevalent worldwide. This syndrome results from intricate interactions between genetic and environmental factors. Obesity, particularly abdominal, is a major contributor, affecting insulin tolerance. Abdominal fat releases adipokines, disrupting glucose physiology. Around 50% of type 2 diabetes patients are obese. Aging, family history, childhood obesity, poor diet, sedentary lifestyle, stress, drug side effects, infections (such as staphylococcus), hypertension, and elevated serum lipid and lipoprotein levels are also implicated in causing type 2 diabetes. The rising prevalence in children and adolescents is linked to increasing childhood obesity over the past two decades [7].

- **Gestational Diabetes**

During pregnancy, hormones crucial for placental development create insulin resistance in the mother, necessitating up to three times more insulin for glucose energy conversion. This leads to Gestational Diabetes, raising blood glucose levels. The condition impacts both mother and baby, causing the baby's pancreas to produce excess insulin, potentially resulting in respiratory issues or hypoglycemia at birth [8].

III. TREATMENT AND MANAGEMENT

Possessing comprehensive knowledge about diabetes is crucial, given its incurable nature but manageable outcomes. Successful diabetes management primarily rests on the patient's shoulders, involving their commitment to dietary choices, regular exercise, and medication adherence. Ongoing advancements in diabetes research contribute to more effective methods for controlling the condition and addressing potential complications. Staying informed about these developments empowers individuals to make informed decisions, enhancing their ability to navigate the complexities of diabetes management and lead a healthier

life.

Hence it includes:-

- Enhanced Insulin Therapies: New and improved insulin formulations, along with external and implantable insulin pumps, offer effective management of elevated blood sugar levels while minimizing allergic reactions.
- Oral Hypoglycaemic Drugs: Specifically designed for type 2 diabetes, oral hypoglycaemic medications contribute to controlling the condition.
- Advanced Blood Glucose Monitoring: The introduction of advanced devices for self-blood glucose monitoring and the Haemoglobin A1C laboratory test provides accurate measurements, offering insights into blood glucose control over the previous three months.
- Targeted Organ Treatments: Improved accessibility to treatments specifically addressing the impact of diabetes on various organs ensures more effective management of the condition's effects on the body [3].

Diabetes is a chronic, incurable condition, managed through medication, exercise, and diet control to maintain blood glucose within suitable limits. Education on potential complications is crucial. Oral hypoglycemic apply to type 2, while type 1 relies on insulin. Lifestyle changes and medication address cardiovascular and cholesterol risks. Insulin management, either regular or synthetic, remains vital for type 1, with modern insulin pumps providing continuous monitoring and preset insulin release for optimal glucose management [1].

IV. HERBAL DRUGS FOR THE TREATMENT OF DIABETES

Despite significant strides in synthetic medicinal chemistry over the past century, various diseases, including infectious, chronic, or emerging ones, still lack successful cures. The treatment of these conditions remains challenging due to the absence of effective and safe drugs capable of providing sustained clinical, biochemical, and definitive cures [9].

In many developing nations, herbal medicine, being an affordable healthcare option, is often the primary recourse. Developed countries also encourage the use of herbal medicine for chronic diseases, driven by concerns about the adverse effects of chemical drugs, with natural remedies appearing to offer milder approaches to disease management [10].

Herbal medications offer advantages such as easy availability, minimal side effects, and cost-effectiveness, making the quest for traditional remedies increasingly significant. Modern society is increasingly embracing herbal drugs, with the perceived safety of herbal origins driving this trend. The marketing strategy for any herbal product is crucial in today's context, as people generally consider herbal origin synonymous with safety. Throughout history, plants have consistently provided a rich source of drugs, with numerous medications directly or indirectly derived from plant sources [11].

Numerous plants have been examined for their antidiabetic properties using modern experimental techniques. Various plant-derived constituents, such as glycosides, alkaloids, polysaccharides, peptidoglycans, hypoglycans, steroids, guanidines, glycopeptides, terpenoids, amino acids, and inorganic ions, show promise in treating type 2 diabetes mellitus [12].

Metformin, a prevalent hypoglycemic drug, finds its origins in the traditional utilization of Galega officinalis. Despite this historical connection, it is crucial to exercise caution, particularly in cases of type 1 diabetes mellitus. The incorporation of hypoglycemic plants in treatment can introduce potential risks, potentially resulting in hypoglycemic accidents, especially in inadequately managed individuals with type 2 diabetes. It underscores the need for careful consideration and monitoring when implementing plant-derived remedies in diabetic care, emphasizing the importance of comprehensive and individualized approaches to diabetes management [13].

The ethnobotanical data highlight various plants with potential antidiabetic properties. This review specifically identifies medicinal plants with hypoglycemic effects, outlining their mechanisms of action. Examples include *Allium sativum, Artemisia pallens, Azadirachta indica, Bauhinia forficata, Eucalyptus*

globules, Gymnema sylvestre, Hibiscus rosa-sinesis, Ipomoea batatas, Ricinus communis, Trigonella foenum, etc. Table 1 presents key herbal plants and their active principles with anti-diabetic potential, offering valuable insights into their medicinal properties.

Allium sativum

In the case of *Allium sativum*, when 0.25 gm/kg of allicin (extracted from *A. sativum*) was orally administered, it induced hypoglycemia in mildly diabetic rabbits, comparable to tolbutamide. However, this effect was not observed in severely diabetic animals. Traditionally, the fruit of this plant is employed as an anti-diabetic remedy in the Mediterranean region. Additionally, the aqueous extract of its fruit demonstrated a dose-dependent enhancement in insulin release from isolated islets [14, 15].

Artemisia pallens

Artemisia pallens exhibited an anti-hyperglycemic effect in a dose-dependent manner, with doses of 100, 500, and 1000 mg/kg, observed in glucose-fed hyperglycemic and alloxanized rats (administered 60 mg/kg intravenously). The study demonstrated the potential of *Artemisia pallens* to mitigate elevated blood glucose levels in a dosage-dependent fashion in experimental rat models [16].

Azadirachta indica

Azadirachta indica displayed both hypoglycemic and anti-hyperglycemic effects in normal, glucose-fed, and streptozotocin-induced diabetic rats. Notably, the pharmacological activity of the plant remains consistent regardless of the timing of administration, either before or after alloxan administration. *Azadirachta indica* operates by impeding the influence of epinephrine on glucose metabolism, ultimately enhancing peripheral glucose utilization [17].

Bauhinia forficate

Bauhinia forficata, derived from fresh leaves, it demonstrates hypoglycemic activity and belongs to the Caesalpiniaceae family. Initial observations of its antidiabetic effects trace back to Juliani in 1941. M.T. Pepato et al. (2002) concocted a decoction from fresh leaves, administering it to rats with streptozotocin-induced diabetes [18].

Eucalyptus globules

The aqueous extract of *Eucalyptus globules*, at a concentration of 0.5 gm/L, demonstrated an augmented utilization of peripheral glucose in mouse abdominal muscle. Additionally, it exhibited a gradual improvement in insulin secretion from the clonal pancreatic beta cell line, reaching a considerable percentage enhancement [19].

Gymnema sylvestre

Gymnema sylvestre showcased noteworthy effects in a study where rats were orally administered powdered leaves (500 mg/rat) for ten days. This treatment significantly thwarted intravenous beryllium nitrate-induced hyperglycemia in the rats, normalizing glucose levels within four days, compared to the untreated group, which required ten days. Interestingly, in normal rats receiving daily feedings of *G. sylvestre* leaves for 25 days, there was no significant occurrence of hypoglycemia [20, 21].

Hibiscus rosa-sinesis

Hibiscus rosa-sinensis exhibited a subtle yet notable hypoglycemic effect at the 120-minute mark in glucose-loaded rats. With daily administration of the same dose over seven days, it demonstrated a significant saving in blood glucose levels at 30, 90, and 120 min after glucose loading in normal rats [22].

Ipomoea batatas

Ipomoea batatas effectively lowers hyperinsulinemia in Zucker fatty rats, resulting in reductions of 23%, 26%, 60%, and 50% after 3, 4, 6, and 8 weeks, respectively. Notably, after 7 weeks of treatment, there is a discernible inhibition of blood glucose levels following glucose loading, accompanied by pancreatic beta cell degranulation and a decrease in insulin resistance [23].

Ricinus communis

Ricinus communis, the castor oil plant, is a traditional diabetes remedy in India. Its ethanolic root extract showed significant hypoglycemic effects in rats, especially at 500 mg/kg. Fraction R18 displayed notable glucose reduction, with continuous administration for 20 days normalizing levels, improving insulin, lipid profile, and body weight. Further research is needed to unveil Ricinus communis' potential as a phytomedicine for diabetes [12, 24].

Trigonella foenum

In various studies involving experimentally induced diabetes in rats, dogs, mice, as well as both insulin-dependent and non-insulin-dependent diabetic human volunteers, *Trigonella foenum*, (fenugreek) seeds have been shown to exhibit a hypoglycemic effect [25, 26].

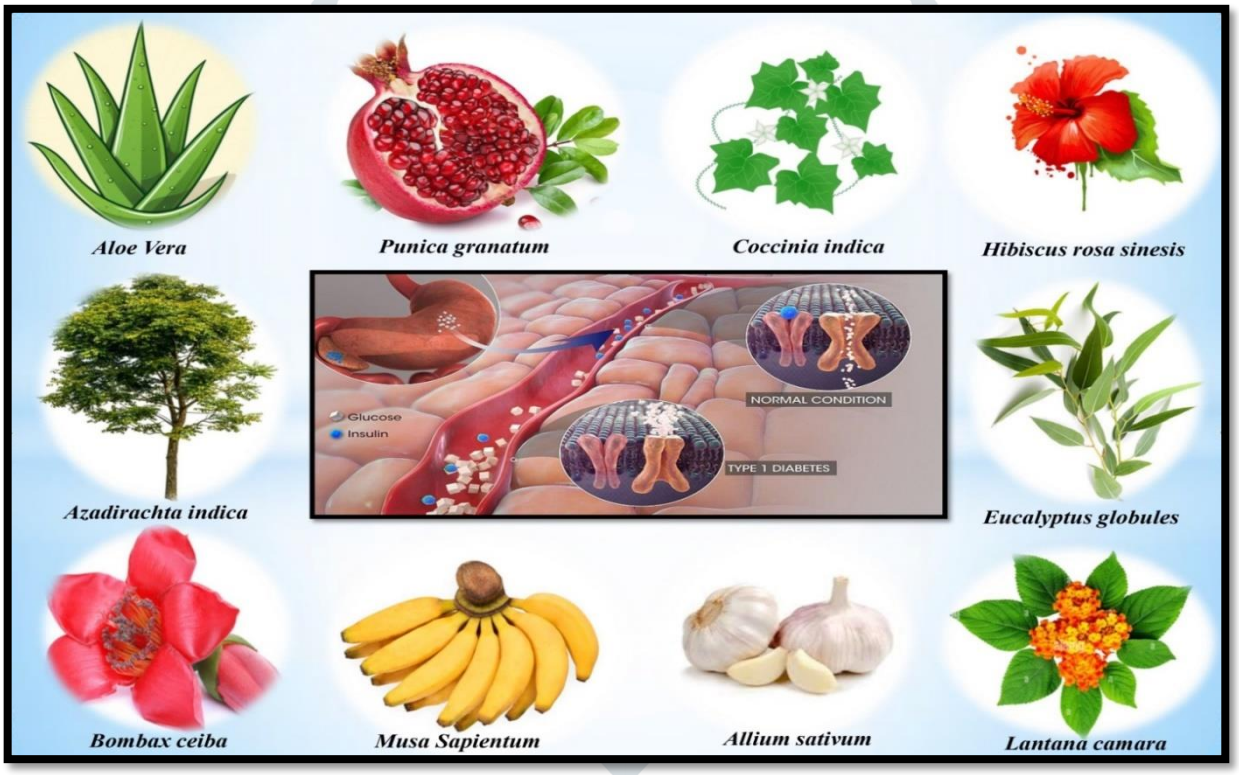

Fig.1: Herbal Products Commonly used in diabetes

Table 1. The List of Herbal Drugs which Possess Anti Diabetic Potential

Botanical name	Family	Parts used	Main Active components	Ref.
Aegle marmelose	Rutaceae	Root bark	Imperatorin, aegelin, lupeol	[27]
Allium cepa	Amaryllidace	Herb	Allicin, quercitin, fisetin	[28]

Allium sativum.	Alliaceae	Bulbs	Allyl propyl disulphide, allicin	[14], [15]
Aloe vera	Liliaceae	Leaves	Aloin, aloe-emodin, barbaloin	[29], [30]
Areca catechu	Arecaceae	Seed	Arecaine and arecoline	[31]
Artemisia pallens	Asteraceae	Leaves and flowers	Germacranolide	[16]
Asparagus racemo susa	Liliaceae	Tender-shoots	Asparagine, arginine, tyrosine	[12]
Azadirachta indica	Meliaceae	Leaf & seed	Azadirachtin and nimbin	[17]
Bauhinia forficata	Leguminosae	Leaves	Astragalin, kaempferitrin	[18]
Berberis aristata	Beriberidaceae	Root, Bark	Berberine, berbamine	[12]
Beta vulgaris	Amaranthaceae	Root	Phenolics, betacyanins	[32], [33]
Bombax ceiba	Bombacaceae	Leaves	Bomcibone, scopoletin	[34]
Cajanus cajan	Fabaceae	Seed	Himachalene, stilbenes	[35], [36]
Cannabis sativa	Cannabaceae	Leaf extract	Cannabidiol	[13]
Cinnamomum tamala	Lauraceae	Decoction of stem bark	Camphene, myrcene, limonene	[37]
Coccinia indica	Cucurbitaceae	Leaves	Asparagine, tyrosine, aspartic acid	[38], [39]
Emblica officinalis	Phyllanthaceae	Fruit	Gallic acid, rutin and quercetin	[40]
Eucalyptus globules	Myrtaceae	Leaves	1,8-cineole, p-cimene, a-pinene	[19]
Eugenia uniflora	Myrtaceae	Leaves	β-pinene, D-limonene, O-cymene,	[41]
Ficus benghalenesis	Moraceae	Bark	Leucodelphinidin and leucopelargonin	[42], [43]
Ficus racemosa	Moraceae	Fruit Juice	Lanosterol, triterpene-glauanol	[37]
Gymnema sylvestre	Asclepiadaceae	Leaves	Dihydroxy gymnemic triacetate	[20], [21]
Hibiscus rosa sinesis	Malvaceae	Shrub	Anthocyanins and quercetin	[22]
Ipomoea batatas	Convolvulaceae	Root	Batatinoside I, citrusin, scopoletin	[23]
Lantana camara	Verbenaceae	Leaves	Lantanoside, lantanone	[44]
Mangifera indica	Anacardiaceae	Leaves	Lysine, leucine, cysteine, valine, arginine, and methionine	[45], [46]
Momordica charantia	Cucurbitaceae	Leaves	Charantin, sterol	[47]
Morus alba	Moraceae	Leaves	Rutin, apigenin, and quercetin	[48], [49], [50]

Murraya koeingii	Rutaceae	Leaves	Linalool, myrcene, allo-ocimene, α-terpinene	[34]
Musa Sapientum	Musaceae	Flowers	Phytol, octadecatrienoic acid, hexadecanoic acid	[51]
Nelumbo nucifera	Nelumbonaceae	Rhizome	Neferine and Liensinine	[52]
Ocimum sanctum	Labiatae	Whole plant	Eugenol	[53], [54], [55]
Panax quinquefolius	Araliaceae	Root	Ginsenosides, protopanaxadiol	[37]
Phyllanthus niruri	Phyllanthaceae	Whole Plant	Quercetin rhamnoside, quercetin glucoside, gallic acid, and geranin	[56]
Picrorrhiza kurroa	Scrophulariaceae	Herb	Cucurbitacins, phenolics	[57]
Psidium guajava	Myrtaceae	Ripe Fruit	Guajanoic acid, beta-sitosterol, uvaol, oleanolic acid,	[58]
Punica granatum	Lythraceae	Fruit	Punicalagin, punicalin	[59], [60]
Quercus lanata	Fagaceae	Stem bark	Vanillin and Quercetin	[37]
Ricinus communis	Euphorbiaceae	Root	Ricinolic acid	[61]
Salacia oblonga	Celastraceae	Root bark	Kotalanol and salacinol	[62]
Salacia reticulata	Celastraceae	Root bark	Dulcitol leucopelargonidin, iguesterin, epicatechin	[63]
Saraca asoca	Fagaceae	Dry flower	Ursolic acid, β-setosterol, Lupeol	[64]
Syzigium cumini	Myrtaceae	Seed	Ellagic acid, isoquercetin, kaemferol and myrecetin	[65]
Tinospora cordifolia	Menispermaceae	Root	11- hydroxymustakone, N-formylannonain, magnoflorine,	[66], [67]
Trigonella foenum graecum	Fabaceae	Seed	Trigonelline, oleic acid, linoleic acid	[25], [26]
Vinca rosea [Ca tharanthus roseus]	Apocynaceae	Leaves	Vinblastine, vinorelbine, vincristine	[61]
Withania somnifera	Solanaceae	Whole Plant	Somniferine and withananine	[61]
Zingiber officinale	Zingiberaceae	Rhizome	Gingerol, zingerone, and paradol.	[12]

V. CONCLUSION

In this current investigation, it was discovered that over 100 plant species from various families are employed globally as antidiabetic agents. This leads us to assert that, even in contemporary times, herbal medicine remains the predominant choice for diabetes treatment. The effectiveness of these ethno medicinal plants should undergo pharmacological validation. Some antidiabetic plants may enhance their impact by stimulating beta cell function or quantity, consequently increasing insulin release. Notably, many widely used modern drugs, such as aspirin, anti-malarials, anti-cancer medications, and digitalis, trace their origins back to plants. Despite an estimated 250,000 higher plants, less than 1% has been pharmacologically screened, particularly concerning diabetes mellitus (DM). Therefore, exploring herbal medicine options for

diabetes is advisable. Our ongoing efforts focus on establishing the scientific foundation for the use of specific plants in treating DM.

The use of traditional remedies in the sampled population doesn't imply fatalism or non-compliance with modern medicine but reflects the patients' efforts to incorporate therapies believed to be effective for maintaining good health. Consequently, the utilization and efficacy of local therapies merit further investigation.

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