Review on Herbal Antidiabetic Plants

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ABSTRACT-
Diabetes mellitus is found in all parts of the world and is becoming a serious threat to mankind health. This disease affects people all over the world and is a big health concern. This disease is caused by the deficiency of production of insulin by the pancreas, which results in increase or decrease in concentration of glucose in the blood. There are many medicines available to control it, but total recovery from diabetes has not been reported up to this date. Some chemical agents have severe side effects. Alterative to these synthetic agents, many herbal plants/natural plants with hypoglycemic properties are known from across the world. The World Health Organization known 21,000 plants used as medicine worldwide. Lots of people, about 60 percent, use traditional plant-based medicines. This review focuses on Indian herbal drugs and plants used in the treatment of diabetes. Especially in used in India. Diabetes is an important human ailment afflicting many from various walk of life in different countries. In India it is proving to be a major health problem, especially in urban areas. The herbal treatment are liked because they have fewer, less side effects and cost less. A list of some medicinal plants with proven antidiabetic and related beneficial effects and herbal drugs are used in antidiabetic treatment are include Allium sativum, Azadirachta indica, stevia rubidana, Psidium guajaval, Cinamonum zeylanicum, Zingiber officinale, Momordica charantia, Ocimum sanctum linn, Syzygium cumini.

KEYWORDS- Diabetes mellitus, antidiabetic drugs, Medicinal plants, Allium sativum, Azadirachta Indica, stevia rubidana, Psidium guajaval, Cinamonum zeylanicum, Zingiber officinale, Momordica charantia, Ocimum sanctum linn, Syzygium cumini.

I. INTRODUCTION
Our bodies have ways to fight damage caused by certain molecules, but sometimes its not enough, leading to diseases like diabetes. This illness affects a lot of people and is expected to keep increasing. The body struggle with insulin, which controls blood sugars. The most common type, type 2, happens when the body does not make or use insulin properly. The world health organization says that by 2025, there might be around 300 million or more people with diabetes. Right now, treatments include insulin, and some pills, but they can have serious side effects, so, that scientists are looking for better and safer medicines for diabetes. One enzyme, aldose reductase, plays a role in diabetes complications by causing substances called sorbitol to build up in the body, leading to problems like cataracts and nerve damage. Some plants have been found to help lower blood sugar, and researchers are studying how they work. These plants have natural substances that might act like insulin or help with how insulin works. Lots of plants—more than 400 kinds—have been looked at for their ability to lower blood sugar. Scientists are interested in these plants because they contain different natural medicines. These compounds include things like glycosides, alkaloids, and flavonoids, which are believed to have an effect on diabetes.

CLASSIFICATION OF DIABETES MELLITUS:
1. β- cell destruction (Type 1 diabetes - IDDM) (a) Immune mediated (b) Idiopathy
2. Insulin resistance (Type 2 diabetes - NIDDM)
3. Genetic defects of β-cell function (a) Glucokinase (b) Hepatocyte nuclear transcription factor – 4 (c) Glucokinase promoter factor (d) Mitochondrial DNA (e) Proinsulin or insulin conversion
4. Genetic defects in insulin processing or insulin actions defects in (a) Proinsulin conversion. (b) Insulin gene mutation (c) Insulin receptor mutation
5. Exocrine pancreatic defects
6. Endocrinopathy (a) Acromegaly (b) Cushing syndrome (c) Hyperthyroidism (d) Pheochromocytoma (e) Glucocanoma
7. Infections (a) Cytomegalovirus (b) Coxsackievirus
8. Drugs (a) Glucocorticoid (b) Thyroid hormone (c) Thiazides (d) Phenyoins
9. Genetic syndrome associated with diabetes (a) Down’s syndrome (b) Kleinfelter’s syndrome (c) Turner’s syndrome
10. Gestational diabetes mellitus

CAUSES OF DIABETES:
Multi-factorial, involving several predisposing conditions and risk factors. In many cases genetics, habits and environment may all contribute to a person’s diabetes.
A. Type 1 Diabetes:
• happens when the body’s defense system attacks the cells in the pancreas that make insulin
• Family history might make someone more likely to get it, but it’s not as common as with Type 2 diabetes.
• Some infections might also play a role.
• It’s seen more in certain ethnic groups and slightly more in men than women.
B. Type 2 Diabetes:
• Things like high blood pressure, high fat in the blood, and giving birth to a big baby can increase the risk.
• Eating lots of fatty foods, drinking a lot, not moving much, being overweight, and getting older can also lead to Type 2 diabetes.

SIGNS AND SYMPTOMS:
Early detection and treatment of diabetes can decrease the risk of developing the complications of diabetes. The following symptoms of diabetes are typical. However, some people with type 2 diabetes have symptoms so mild that they go unnoticed. Common symptoms of diabetes:
• Feeling very thirsty
• Feeling very hungry - even though you are eating
• Extreme fatigue
• Blurry vision
• Cuts/bruises that are slow to heal
• Weight loss - even though you are eating more (type 1)
• Tingling, pain, or numbness in the hands/feet (type 2)

Table 1: Sign & symptoms of Diabetes mellitus
<table>
<thead>
<tr>
<th>Prediabetes</th>
<th>Type 1 diabetes</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>No symptoms</td>
<td>Increased or frequent urination</td>
<td>Increased urination</td>
</tr>
<tr>
<td></td>
<td>Increased thirst</td>
<td>Increased thirst</td>
</tr>
<tr>
<td></td>
<td>Increased appetite</td>
<td>Increased appetite</td>
</tr>
<tr>
<td></td>
<td>Increased fatigue</td>
<td>Fatigue</td>
</tr>
</tbody>
</table>

COMPLICATIONS OF DIABETES:
The complications of diabetes mellitus are far less common and less severe in people who have well-controlled blood sugar levels.
1. Micro vascular Complications-
   • Diabetic Retinopathy
   • Diabetic Nephropathy
   • Diabetic Neuropathy
2. Macro vascular Complications-
   • Atherosclerosis
   • Cardiovascular Disease(CVD)
   • Stroke

PATHOPHYSIOLOGY OF DIABETES:
Normal insulin release: The pancreas releases insulin in response to food, especially when there’s glucose in the blood from the food you’ve eaten. Insulin helps cells take in glucose from the blood to use as energy.
Glucose as energy: Glucose is a key energy source for our body. It comes from carbs in food and is used right away or stored for later use.
Role of insulin: Insulin helps cells absorb glucose, use it for energy, or store it. When insulin is low, the liver releases stored glucose back into the blood.
Glucagon’s role: Glucagon does the opposite of insulin. It raises blood glucose levels by releasing stored glucose when needed.
Impact of insulin issues: If there’s not enough insulin, or the body doesn’t respond well to it, glucose can’t enter cells properly. This leads to high blood sugar levels and problems with the body’s normal functions.
Consequences of high blood sugar: High blood sugar affects the kidneys, causing glucose in the urine (glycosuria) and increased urine production (polyuria), among other metabolic issues like poor protein synthesis and acidosis.

DIABETES DIAGNOSIS:
The blood glucose levels of a healthy man are 80mg / dL on fasting and up to 160 mg / dL in the
postprandial state. A number of laboratory tests are available to confirm the diagnosis of diabetes.

1. Finger stick blood glucose.
2. Fasting plasma glucose.
3. Oral glucose tolerance test.
4. Glycosylated haemoglobin or haemoglobin A1C.

**DIABETES MEDICATIONS:**

Many different types of medications are available to help lower blood sugar levels in people with type 2 diabetes. Each type works in a different way. It is very common to combine two or more types to get the best effect with fewest side effects.

- **Sulfonylurea:** These drugs stimulate the pancreas to make more insulin.
- **Biguanides:** These agents decrease the amount of glucose produced by the liver.
- **Alpha-glucosidase inhibitors:** These agents slow absorption of the starches and glucose.
- **Thiazolidinediones:** These agents increase sensitivity to insulin.
- **Meglitinides:** These agents stimulate the pancreas to make more insulin.
- **D-phenylalanine derivatives:** These agents stimulate the pancreas to produce more insulin more quickly.
- **Amylin synthetic derivatives:** Amylin is a naturally occurring hormone secreted by the pancreas along with insulin. An amylin derivative, such as pramlintide (Symlin), is indicated when blood sugar control is not achieved despite optimal insulin therapy.
- **Incretin mimetics:** Exenatide (Byetta) was the first incretin mimetic agent approved in the United States. It is indicated for diabetes mellitus type 2 in addition to metformin or a sulfonylurea when these agents have not attained blood sugar level control alone.
- **Insulins:** Synthetic human insulin is now the only type of insulin. It is less likely to cause allergic reactions than animal-derived varieties of insulin used in the past. Different types of insulin are available and categorized according to their times of action onset and duration. Examples of rapid-acting insulins –
  - Regular insulin (Humulin R, Novolin R)
  - Insulin lispro (Humalog)
  - Insulin aspart (Novolog)
  - Insulin glulisine (Apidra)
  - Prompt insulin zinc (Semilente, slightly slower acting)

Examples of intermediate-acting insulins –

- Isophane insulin, neutral protamine Hagedorn (NPH) (Humulin N, Novolin N)
- Insulin zinc (Lente)
- Insulin glargine (Lantus)
- Insulin detemir (Levemir)
- Extended insulin zinc insulin (Ultralente)

**DIABETES TREATMENT**

Treatment involves medicines, diet, and exercise to control blood sugar and prevent symptoms and problems.

**Diabetes Diet:**

A healthy diet is a key to controlling blood sugar levels and preventing diabetes complications.

- **Diet:** Eat regularly, with balanced meals high in fiber and low in unhealthy fats and sugary foods. If weight loss is tough, ask a professional for help.
- **Exercise:** Even just 20 minutes of walking three times a week helps a lot. It lowers diabetes risk and keeps complications away.
- **Control Blood Sugar:** Keeping your sugar levels stable daily is the best thing for diabetes.
- **Quit Smoking:** Smoking makes diabetes worse. If needed, seek help to quit.
- ** Maintain Healthy Habits:** Keep a healthy weight and keep a log of what you eat, when you take meds, and issues you face.
- **Alcohol:** Limit alcohol as it can mess with blood sugar levels.
- ** Keep Track:** Check blood sugar levels regularly and keep a log of what you eat, when you take meds, and any issues you face.
- **Get Educated:** When diagnosed, your healthcare team will teach you how to manage diabetes.
- **Follow-up:** Stick to the treatment plan, track your blood sugar, and contact your doctor if you have any problems or concerns.
- **Prevention:** For type 2 diabetes, focus on a healthy diet, exercise, limit alcohol, avoiding smoking, take meds if needed for high cholesterol or blood pressure, and consider lifestyle changes to prevent it.

**AYURVEDIC HERBS IN THE TREATMENT OF DIABETES MELLITUS**

Diabetes mellitus in Ayurveda is known as Madhu-meha. Several Ayurvedic herbs have been used in the treatment of Diabetes Mellitus for centuries. In addition to herbs, Minerals find wide application in Ayurvedic Prescription for diabetes. Medicinal herbs like Momordica charantia, Gymnema sylvestre, Enicostemma littorale, Pterocarpus marsupium,
Salacia reticulate, Coccinia gluaca and Trigonella foneum graceum are prescribed as single powder drugs or in combination (poly-Herbal). Scientists have studied the chemical composition of the antidiabetic medicinal herbs used in Ayurveda. The article deals with work done on Indian medicinal plants with antidiabetic potential. (Sadhu, 2005)

How do herbs work?

For most herbs, the specific ingredient that causes a therapeutic effect is not known. Whole herbs contain many ingredients, and it is likely that they work together to produce the desired medicinal effect. The type of environment (climate, bugs, soil quality) in which a plant grew will affect its components, as will how and when it was harvested and processed.

How are herbs used?

For the reasons described in the previous section, eczema, premenstrual syndrome, rheumatoid arthritis, migraine, menopausal symptoms, chronic fatigue, and irritable bowel syndrome, among others. Herbal preparations are best taken under the guidance of a trained professional.

What is the future of herbal medicine?

Although a renaissance is occurring in herbal medicine in the United States, the FDA still classifies herbs as dietary supplements forbids manufacturers to claim that their products are able to treat or prevent specific diseases. In some countries in Europe, however, herbs are classified as drugs and are regulated. The German Commission E, an expert medical panel, actively researches their safety and effectiveness. (Fugh-Berman, 2000)

1. Allium Sativum (Lahsun)-

- Synonyms: Garlic (Eng), Lasan (GuJ), Lasun (Hindi), Lashuna (Sanskrit).
- Biological Source: Garlic consists of ripe bulbs of Allium sativum
- Family: Liliaceae.
- Parts used: Ripe Bulbs.
- Geographical source: Central Asia, Southern Europe, insulin. It also improved diabetic conditions.
- Scientific Classification:
  a. Kingdom: Plantae
  b. Division: Magnoliophyta
  c. Class: Liliopsida
  d. Order: Asparagales
  e. Family: Liliaceae
  f. Genus: Allium
  Chemistry: It contains a wealth of sulphur compounds; most important for the taste is Allicin, which is produced enzymatically from allin. It also contains 65% water, 28% carbohydrate, 2.3% organosulphur compound, 2% proteins, 12% free amino acid (mainly arginine), 1.5% fiber, 0.15% lipids, 0.08% phytic acid, peroxidation better than glibenclamide and insulin. It also improved diabetic conditions. SACS also stimulated in vitro insulin secretion from beta cells isolated from normal rats. Apart from this, Allium sativum exhibits antimicrobial, anticancer and cardioprotective activity.

2. Syzygium Syzygium (Jambul) –

- Synonyms: Black jamun
- Biological source: Jamun, Syzygium Cumini
- Family: Myrtaceae
- Scientific Classification:
  a. Kingdom: Plantae
  b. Division: Magnoliophyta
  c. Class: Magnoliopsida
  d. Order: Myrtales
  e. Family: Syzygium
  f. Genus: Syzygium
  g. Species: Cumini
- Chemistry: The plant is rich in compounds containing anthocyanins, glucoside, ellagic acid, isoquercetin, kaempferol, myricetin, and hydrolysable tannins (1-0-galloyl castalagin and casuarinin).
- The seeds also contain alkaloid jambosine and glycoside jamboline, which slows down the diastatic conversion of bounce into sugar.
- The blood glucose-lowering effect of Eugenia jambolanamay be due to increased secretion of insulin from the pancreas or by inhibition of insulin degradation.
3. Azadirachta Indica - Neem -

Synonym: Limedo (Guj), Neem (Hindi).

Biological source - Neem consists of almost all the part of the plant which are used as drug of Azadirachta indica. It is also known as margosa, Indian Lilac and Azadirachta indica.

Family: Meliaceae

Parts used: Whole plants.

Geographical source - Azadirachta indica is widely distributed throughout India, Pakistan and Bangladesh. That's normal name is neem.

Scientific Classification -

Botanical description - Taxonomic Postion of Azadiractaindica, neem

a. Order- Rutales
b. Suborder- Rutinae
c. Family - Meliaceae
d. Subfamily - Melioidae
e. Tribe - Meliaceae
f. Genus - Azadirachta
g. Species - indica

Chemistry: Nimbidin is major source from seed oil, It is crude bitter principle. It also contain nimbin, nimbinin, nimbidinin, nimbolide, nimbilic acid. Gedunin obtained from neem’s seed. It also contain mahmoodin, Azadirachtin. It also contain some tannins like, Gallic acid. There are also present of Margolonon, Polysaccharide.

Pharmacological study: Researchers least partially reducing diabetics' need for insulin at India's University of Madras in the early 1990s found that high doses (40 gm of dried herb daily) of Azadirachta Indica extracts may actually help to repair or regenerate the pancreas's beta cells, which play a crucial role in the production and secretion of insulin. Few other substances, synthetic or natural, offer such promise for reversing beta cell damage and at least partially reducing diabetics' need for insulin and other drugs. On the other hand, studies indicate that animals that do not have diabetes do not produce more insulin after consuming Azadirachta Indica (Neem).

4. Stevia Rabbudiana -

Synonym - Honey leaf

Biological Source - Stevia rebaudiana Bertoni is the botanical name of stevia. It is a perennial shrub belongs to the (Asteraceae) Composite family. Geographical Source - Stevia is native to Paraguay and Brazil.

Scientific Classification -

a. Kingdom- Plantae
b. Division - Magnoliophyta
c. Class - Magnoliopsida
d. Subclass - Asteridae
e. Order - Asterales
f. Family - Asteraceae
g. Genus - Stevia
h. Species - rebaudiana
i. Commonwealth name - Sweet leaf

Chemistry: Steviol is the basic building block of stevia's Sweet Glucoside: Stevioside and rebaudioside A are constructed by replacing the bottom hydrogen atom with glucose and the top hydrogen atom with two or three linked glucose groups, respectively.

Clinical study: Jeppesen, et al. 2004 Stevioside is present in the plant Stevia rebaudiana Bertoni (SrB). Extracts of SrB have been used for the treatment of Diabetes in, for example, Brazil, although a positive effect on glucose metabolism has not been unequivocally demonstrated. They studied the acute effects of stevioside in type 2 diabetic patients. We hypothesize that supplementation with stevioside To a test meal causes a reduction in postprandial blood glucose. Twelve type 2 diabetic patia...
incremental area under the glucose response curve by 18% (P < .013). The insulinogenic index (AUCi, insulin/AUCi, glucose) was increased by approximately 40% by stevioside compared to control (P < .001). Stevioside tended to decrease glucagon levels, while it did not significantly alter the area under the insulin, glucagon-like peptide 1, and glucose-dependent insulinotropic polypeptide curves. In conclusion, stevioside reduces postprandial blood glucose levels in Type 2 diabetic patients, indicating beneficial effects on the glucose metabolism. Stevioside may be advantageous in the treatment of type 2 diabetes.

5. Momordica charantia: (bitter melon) -
Synonym- Balsam apple, balsam pear, Bitter guard.
• Biological source- Momordica charantia is grown for its fruit, young shoot and edible flower • Scientific name- Momordica charantia
Family- cucurbitaceae Parts used-Whole section of this plant, such as fruit pulp, seeds, leaves and whole plant extracts.
Geographical Sources- Momordica charantia is used more frequently as a hypoglycemic agent in India.
• Scientific classification
  a) Kingdom- plantae
  b) Division- magnoliopsid
  c) Order- cucubitales
  d) Order- cucubitales
  e) Family- Cucurbitaceae
  f) Genus- momoridica
  g) Species- charantia
• Common name- Karla, Bitter guard.
• Chemistry- Antidiabetic constituent Polypeptide-p or p-insulin is an insulin-like - Polypeptide-p. Antidiabetic properties of Bitter melon - Bitter melon is one of the most commonly used vegetable that contains polypeptide-p and is used to control diabetes. Hypoglycemic protein, shown to lower blood glucose levels.

6. Zingiber officinale , Ginger-
Synonym- Adarak, Aal, Zingiber, Zingiberis
• Biological source- ginger herbaceous perennial plant probably native to southeaster Asia, or its pungent aromatic rhizome (underground stem) used as a spice, flavouring, food, and medicine.
Family- zingiberaceae
Parts used- Rhizomes, root, shoot
Geographical Source- It probably originated in southeast asia, it is cultivated in many tropical regions, including Africa, china, India
• Scientific Name-Zingiber officinale
• Scientific classification
  a. Kingdom- plantae
  b. Division- magnoliophyte
  c. Class – liliopsida
  d. Order – zingiberales
  e. Family – zingiberaceae
  f. Gene – zingiber
  g. Species -zingiber officinale.
• Common Name- Ginger, Adarak.
• Chemical constituent -Antidiabetic constituent- Alpha- zingiberene Antidiabetic properties of Ginger- Anti-diabetic effects through restorative effects on pancreatic β-cells, increasing insulin sensitivity, insulin-like action and peripheral utilization of glucose.
7. Cinnamomum zeylanicum, Cinnamon -
• Synonym - Cinnamon bark, Kalmi, Dalchini.
  • Scientific name - Cinnamomum verum.
  • Biological Source - Cinnamon is the dried inner bark of the coppiced shoots of Cinnamomum zeylanicum
Family - lauraceae
Parts used – dried inner bark
• Scientific Classification
  a. Kingdom - Plantae
  b. Division - Magnoliophyta
  c. Class – magnoliopsida
  d. Order – magnoliales
  e. Family - lauraceae.
  f. Genus – cinnamo schaeff
g. Species – cinnom tamala
• Chemistry - Antidiabetic constituent – cinnamaldehyde Antidiabetic properties of Cinnamon- Antidiabetic effects through inhibiting gastro-intestinal enzymes, modulating insulin response and sensitivity, improving glucose uptake, inhibiting gluconeogenesis and increasing glycogen synthesis.
  The main constituents of cinnamon are cinnamaldehyde, cinnamate essential, cinnamic acid, and numerous oils. They all contribute to the odor and to the several biological activities observed with cinnamon. It also contains procyandins tannins, mucilage, and a bit amounts of coumarin. Cinnamaldehyde (trans-cinnamaldehyde) is the foremost constituent in cinnamon bark oil. However, the principal component of leaf oil is eugenol.

8. Psidium guajaval, Guava -
• Synonym - Guajava pyrifera
• Scientific Name - Psidium guajaval
• Biological Source - Guava trees are native to tropical America and are grown in tropical and subtropical areas worldwide. Guava fruits are processed into jams, jellies, and preserves and are common pastry fillings
Family- myrtleaceae
Plant parts used- leaves, bark, whole parts
Geographical sources- It is now cultivated in Southern Florida, Bermuda, and throughout the West Indies from the Bahamas and Cuba to Trinidad, and south to Brazil
• Scientific classification
  a. Kingdom - Plantae
  b. Order – myrtales
  c. Family- myrtalecae
d. Genus -Psidium e. Species- P. guajava.
• Chemistry - Antidiabetic constituent- Polyphenol compound. Antidiabetic properties of Guava leaves- Reduced blood glucose level, increased plasma insulin level in an oral glucose tolerance test, and stimulated activities of some glucose metabolic enzymes.
  Guava contains broad spectrum of phytochemicals including minerals, enzymes, proteins29, sesquiterpenoid alcohols and triterpenoid acids30,31,32, alkaloids, glycosides, steroids, flavanoids, tannins, saponins33,34. Guava is very rich in antioxidants and vitamins and also high in lutein, zeaxanthine and lycopene35,36. The guava leaves contain several chemical constituents such as α-pinene, β-pinene, limonene, menthol, terpenyl acetate, isopropyl alcohol, longicyclene.
Caryophyllene, β-bisabolene, caryophyllene oxide, β-copanene, farnesene, humulene, selinene, cardinene and curcumene, mallic acids, nerolidiol, βsitosterol, ursolic, crategolic, and guayavolic acids, cineol, quercetin, 3-L-4-4-arabinofuranoside (avicularin) and its 3-L-4-pyranoside (essential oil), resin, tannin, eugenol.

9. Ocimum sanctum Linn. (Tulsi)-
Synonym- Holy basil -(Ocimum sanctum) , tulsi
Biological source-It consists of Fresh and dried leaves of ocimum species like ocimum sanctum l, and ocimum basilicum l
Family: Labiatae
Parts used- leaves, roots ,whole plant
Geographical sources- mostly in india, Malaysia, Australia, West Africa and some of the Arab countries.
Scientific classification -
Kingdom : Plantae
Subkingdom : Tracheobionta
Superdivision : Spermatophyta
Division : Magnoliophyta
Class : Magnoliopsida
Subclass : Asteridae
Order : Lamiales
Family : Lamiaceae
Genus : Ocimum
Species : O. sanctum
Chemistry: Volatile oil (containing eugenol and caryophyllene), triterpenoid (rosmarinic acid and ursolic acid) Flavonoids and Saponin.
Tulsi is also known as “the elixir of life” since it promotes longevity. Different parts of the plant are used in Ayurveda and Siddha systems of medicine for prevention and cure of many illnesses and everyday of medicine for prevention and cure of many illnesses and everyday ailments like common cold, headache, cough, influenza, earache, fever, colic pain, sore throat, bronchitis, asthma, hepatic diseases, malar fatigue, skin diseases, wound, insomnia, arthritis, digestive disorders, night blindness and diarrhoea. The leaves are good for nerves and to sharpen memory.

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