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Development of Herbosomes for the Treatment of Diabetes

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ABSTRACT

The main aim of this article is to reduce the adverse effects associated with synthetic drugs which are used to reduce the side effects of diabetes. Diabetes mellitus is a chronic disorder characterized by hyperglycemia because of impaired insulin action, decreased insulin production. Chronic diabetes can cause other health complications which affect arteries, eyes, kidneys and nerves. There are multiple therapies available to treat diabetes, but total recovery from diabetes may not possible. The major disadvantage of the allopathic drugs have some adverse effects such as renal impairments, mal-absorption, diarrhea and abdominal bloating. The anti-diabetic medicines from plants have a similar mechanism of action as allopathic drugs and lessside effect with low cost. A list of medicinal plants with proven anti diabetic and related beneficial effects of herbal drugs used in treatment of diabetes such as Allium sativum, Eugenia jambolana, Ocimum sanctum, Acacia arabica, Allium cepa, aloe vera, aloe barbadensis and azadirachta indica etc.

Keywords: *anti diabetic, hyperglycemia, allopathic drugs, herbs.*

INTRODUCTION

Diabetes mellitus is a chronic metabolic disorder exhibited as the presence of higher concentrations of glucose in the blood either because of improper production of insulin from pancreas or reduced insulin production (1).According to statistics, 2.8% of the world's population suffer from the disease and it is expected to increase to more than 5.4% by 2025(2). Diabetes requires early diagnosis, treatment, and way of life changes (3). Nowadays, different treatments, such as insulin therapy, pharmacotherapy and diet therapy are available to control the disease. There are several types of glucose-lowering drugs that exert anti-diabetic effects through different mechanisms (4). These mechanisms include stimulation of insulin secretion by sulfonylurea and meglitinides drugs, increasing of peripheral absorption of glucose by biguanides and thiazolidinedione delay in the absorption of carbohydrates from the intestine by alpha-glycosidase and reduction of hepatic gluconeogenesis by biguanides(5).These treatments have some disadvantages, such as drug resistance (reduction of efficiency), side effects, and even toxicity. Nowadays, many treatments that involve the use of medicinal plants are recommended(6). Mostly plants contain carotenoids, flavonoids, terpenoids, alkaloids and glycosides can be used as Anti-diabetic effects(7).The Anti-hyperglycemic effects that results from treatment with plants are often due to their ability to improve the performance of pancreatic tissue, which is done by increasing insulin secretions or reducing the intestinal absorption of glucose. The main purpose of this article is to introduce a number of effective medicinal plants used for treating diabetes and other mechanisms of plant compounds used to reduce glucose levels and increase insulin secretion (6).

TYPES OF DIABETES MELLITUS

Type1 Diabetes

It is known as IDDM, juvenile-onsetdiabetes or immune-mediated diabetes. It cause due to autoimmune damage of the pancreatic β-cells, which areinsulin-producing cells (8).

Type 2 Diabetes

It is known as NIDDM or adult-onset diabetes. It is cause by insulin resistance with relativeinsulin deficit to a mainly insulin secretary deficiency(9).

Gestational Diabetes

This type of diabetes cause inpregnant women, who never had diabetes earlier, buthave a high blood glucose level during pregnancy. It may lead development of type 2 diabetes mellitus between 5 to10 years after delivery(10).

NIDDM: Non-insulin-dependent diabetes mellitus, IDDM: Insulin-dependent diabetes mellitus(11).

Signs and Symptoms of Diabetes Mellitus

- Repeated urination
- increased thirst
- weight loss
- hunger
- blurred vision
- fatigue
- Feeling very tired most of the time
- Very dry skin
- Weight gain.
- Nausea
- Slow healing of cuts and wounds(12)

Pathophysiology

Insulin is the main hormone to control the uptake of glucose from the blood into various cells of the body, chiefly liver, muscle as well as adipose tissue. Beta cells (β-cells), found in the islets of Langer hans in the pancreas, release insulin into the blood in response to rising levels of blood glucose, typically after eating. About 2/3rd of the body's cells use insulin for glucose absorption from the blood for use as fuel, for changes to other needed molecules. Decrease in the release of insulin from the beta cells and the breakdown of glycogen to glucose is an outcome of lower glucose levels. The hormone glucagon frequently controls this process, which acts in the converse manner to insulin. If the amount of insulin available is inadequate, if cells respond wildly to the effects of insulin (insulin tactlessness or insulin resistance), or if the insulin itself is defective, then glucose will not be absorbed properly by the body cells that require it, and it will not be stored properly in the liver and muscles. The net result is dependable elevated intensity of blood glucose, decrease protein synthesis, plus additional metabolic unbalance, such as acidosis. While the glucose concentration in the blood vestiges elevated above time, the kidneys will achieve a portal of reabsorption, excretion in the urine (glycosuria)(13).

Causes

- Due to high bloodpressure
- Smoking
- Hereditary
- Overweight and high cholesterol levels and
- Lifestyle

Diagnosis

Following tests are used in diagnosing of diabetes:

Random Plasma Test

This is the simplest test that requires no fasting previous to the test. Blood glucose of 200 or more than 200 mg/dl possibly particular diabetes but have to be repeated again(15).

Fasting Plasma Glucose Test

The test needs eight hours fasting. More than 126 mg/dl blood glucose on two or more tests carried out on various days confirm a diabetes diagnosis (16).

Oral Glucose Tolerance Test

This test is carry out when random plasma glucose test is 160-200 mg/dl and the fasting plasma test is 110-125 mg/dl. This blood test approximates body's response to glucose is estimated. Fasting of at least eight but not more than 16 hours is need in this test. Fasting glucose intensity is determined furthermore provide 75 gm of glucose, 100 gm for pregnant women. Each 30 minutes to 1 hour for 2 or 3 hours the blood is tested. If the glucose level at 2 hours is less than 140 mg/dl, then this test is normal. A diabetes diagnosis is confirmed with the fasting level of 126 mg/dl or greater and 2-hours glucose level of 200 mg/dl or greater (15).

HbA1C (A1C or glycated hemoglobin test)

This test can be used for the diagnosis of both pre-diabetes and diabetes. Average blood glucose control for the past 2 to 3 months is calculated. Moreover, this test is more suitable as no fasting is required. When the A1C is 6.5% or greater, diabetes is diagnosed (15).

Fructosamine Test

The important component of plasma proteins is albumin. Since albumin too includes open amino clusters, non-enzymatic reaction among glucose within plasma occurs. Thus, glycated albumin be able to equally stay up like a indicator to examine blood glucose. Glycated albumin is generally taken to present a fair measure of regular blood glucose concentration greater than a time of 1 to 3 weeks(14).

Mechanisms of Action of Herbal Anti-Diabetic Agents are

- Adrenomimeticism, pancreatic β-cell potassium channel blocking, cyclic adenosine mono-phosphate stimulation

- Reduced in insulin resistance
- Decreased lipid peroxidation (16)

CHEMICAL CATEGORIZATION OF VARIOUS PHYTOCONSTITUENTS

SI.NO	Phytoconstituents	Targeted metabolic Pathways	Plant source
A 1	**Alkaloids** Barberin	Glucose transport, Carbohydrate digestion and absorption, DPP-IV inhibition	Tinosporacordifolli ia, barberisaristata
2	Catharanthine,vindoline, vindolinene vinblastine, vincristine	Free-radical scavenging action	Cathanthrusroseus, Vincarosea
3	Stolon [4,5-dimethyl-3-hydroxy-2(5H)-furanone], trigonelline, gentianine, carpaine compounds	Glucose transport, carbohydrate digestion and absorption	Trigonellafoenum graecum
4	Ginkgolides	Insulin secretion	Ginkgo biloba
5	Allylpropyl disulfide	Glycogen synthesis, insulin secretion	Allium sativum
6	Aegelin, marmesin, marmelosin	Regeneration of pancreatic beta cells and insulin secretion	Aeglemarmelos

Amino Acids, Amines and Carboxylic Acid Derivatives

1	**Allicin, apigenin, alliin**	**Cholesterol synthesis, glycogen synthesis**	**Allium sativum**
2	Gurmarin, betaine, choline, Tri-methylamine	Regeneration of pancreatic βcells and insulin secretion	Gymnema sylvestre
3	(–) Hydroxycitric acid	Insulin secretion	Garciniacambogia, Gymnemasylvestre
4	Ferulic acid	Free radical scavenging activity, insulin secretion	Curcuma longa
5	Leucine, isoleucine, alanin	Insulin secretion	Aloe Vera
6	Mallic acid, chlorogenic acid	Krebs cycle	Carallumaedulis, Syzygiumcumini, Acacia Arabica
7	Nitrosamines	Carbohydrate digestion and absorption	Areca catechu

Anthranoids

1	**Aloin,barbaloin, isobarbaloine, aloetic acid, aloe-emodin, emodin, cinnamic acid, crysophanic acid**	**Insulin secretion and synthesis**	**Aloe Vera, Cassia tora**
2	Vicine	Insulin secretion	Momordicacharantia
3	Torachrysone, toralactone, rhein, alaternin	Insulin secretion	Cassia tora
4	Camphor, eugenol, trans-β-ocimene, geraniol, α-pinene, limonene, p-cymene, 1,8-cineole, thujone	Insulin secretion, Regeneration of pancreatic β cells	Ocimumcanum, Coriandrumsativum, Artemisia roxburghiana, Syzygiumaromaticum

Carbohydrates

1	**Glucomannan**	**Insulin secretion, carbohydrate digestion**	**Aloe Vera**
2	Caryophylline	Insulin secretion, carbohydrate digestion and absorption	Ocimum sanctum, Syzygiumaromaticum
3	Protein-bound polysaccharide	Insulin secretion, carbohydrate digestion and absorption	Alpinia galangal, AloeVera, Ocimum sanctum
4	Guar gum, pectin and pectin fibres, mucilaginous fibre	Glucose transport, carbohydrate metabolism, stabilizing agents	Trigonellafoenumgraecum, Citrus sinensis, Cocciniaindica

5	Cellulose, mannose	Carbohydrate digestion and absorption	Aloe Vera
6	D-threitol, D-arabinitol, palmitic acid	Carbohydrate digestion and absorption	Hericiumerinaceus
7	L-arabino-D-xylan, cinnzeylanin, cinnzeylanol, D-glucan	Carbohydrate digestion and absorption	Cinnamomumzeylanicum
8	Mucopolysaccharide	Carbohydrate metabolism, cholesterol synthesis	Opuntiaficusindica

Glycosides

1	**Gymnemic acid, gymnemosides**	**Regeneration of pancreatic β cells and insulin secretion**	**Gymnemasylvestre**
2	Vin α-ginsenoside R3	Insulin secretion	Panaxquinquefolium
3	Astragalin,scopolin, skimmin, roscoside II	Regeneration of pancreatic β cells and insulin secretion	Morus alba
4	C-glycosides	Glucose transport, carbohydrate metabolism	Trigonellafoenumgraecum
5	Momordin, momordicine, charantin	Insulin secretion, glycogen synthesis	Momordicacharantia
6	Tinosporine, cordifolide, tinosporide, cordifole, columbin	Cholesterol synthesis, glycolysis	Tinosporacordifollia, Tinosporacrispa
7	Momorcharaside A and B, , momorcharin A and B	Insulin secretion, glycogen synthesis	Momordicacharantia
8	Cucurbitacin B, isocucurbitacin B	Insulin secretion, glycogen synthesis	Helicteresisora
9	Momordin-a, luffin-a	Insulin secretion, glycogen synthesis	Luffacylindnica
10	Kotalanol, salacinol	Insulin secretion, glycogen synthesis	Salacia reticulate, Salaciaoblonga

Flavonoids

1	**Chrysin, isoquercitrin**	**Insulin secretion**	**Morus alba**
2	Epigallocatechin-gallate, gallocatechin, epicatechin, (+) catechin, (−) epicatechin	Free-radical scavenging activity, insulinonematic activity	Camellia sinensis, Punicagranatum, Saturejakhuzestanica, Bauhinia forficate
3	Myrciaphenones A and B, myrciacitrins I and II	Insulin secretion	Myrciamultiflora
4	α-Cephalin, myricetin-3'-glucoside, ambrettolide	Insulin secretion	Abelmoschusmoschatus
5	Cytrus bioflavonoids (hesperidin, naringin)	Glycogen synthesis, glycolysis, gluconeogenesis	Camellia sinensis
6	Flavanols, flavones, flavanones	Insulin secretion	Panaxnooginseng
7	Naringenin	Insulin secretion	Camellia sinensis
8	Soy isoflavones (genistein, diadzein)	Lipid and glucose metabolism, PPAR activation	Glycin max, Curcuma longa
9	Proanthocyanidins	Insulinonematic activity	Vitisvinifera
10	α-Terpineol, hexanol	Insulin secretion	Agaricuscampestris
11	Kaempferitrin	Glycolysis	Bauhinia candicans, Bauhinia forficate
12	(+)Catechin, (−) epicatechin, chiorogenicacid, liquiritigenin, isoliquiritigerin	Insulinomematic activity	Phylanthusembelica, Acacia Arabica, Pterocarpusmarsupium, Phylanthusembelica
13	Silymarin, silybin, silychristin, silidianin	HMG Co A suppression	Silybummarianum
14	Kaempferol, isorhamnetin	Free radical scavenging activity	Ginkgo biloba
15	Amarogentin, swerchirin, chirantin, gentiopicrin	Insulin secretion, glycogen synthesis	Swertiachirayita

Minerals, Vitamins and Inorganic Compounds

1	**Zinc**	**Insulin secretion**	**Aloe vera**
2	Vitamin A,E	Free radical scavenging activity	Cucurbitapepo

Peptidoglycans

1	**Fenugreekine.**	**Glucose transport, carbohydrate digestion and absorption**	**Trigonellafoenum graecum**
2	Gluten, taraxacerin	Glucose transport, carbohydrate digestion and absorption	Taraxacumofficinale
3	Glucosamines	Insulin secretion, carbohydrate digestion and absorption	Aloe vera

Saponins

1	**Stigmasterol, quercitol, gymnenic acid IV**	**Regeneration of pancreatic β cells, insulin secretion**	**Gymnemasylvestre**
2	Quinquenoside L3 and L9	Regeneration of pancreatic β cells and insulin secretion	Panaxquinquefolium
3	Andrographolide	Regeneration of pancreatic β cells, insulin secretion	Andrographispaniculata
4	3-O-β-D-glucopyranoside	Regeneration of pancreatic β cells and insulin secretion	Myrtuscommunis
5	3-Hepatadecanone, 8-hexadecenoic acid hexadecenoic acid	Regeneration of pancreatic β cells and insulin secretion	Asparagus adscendens
6	Ginsenosides Rg2, panaxan A, B, C, D, E	Regeneration of pancreatic β cells, free radical scavenging	Panax ginseng
7	Lactucain C	Regeneration of pancreatic β cells, insulin secretion	Lactucaindica

Medicinal Plants with Anti-Diabetic and Related Beneficial Properties

Si.no	Plant Name	Ayurvedic/Common Name/Herbal Formulation	Anti-diabetic And Other Beneficial Effects In Traditional Medicine
1	Annona squamosal	Sugar apple	Hypoglycemic and anti-hyperglycemic activities of ethanolic leaf-extract, Increased plasma insulin level
2	Artemisia pallens	Davana	Hypoglycemic, increases peripheral glucose utilization or inhibits glucose reabsorption
3	Areca catechu	Supari	Hypoglycemic
4	Beta vulgaris	Chukkander	Increases glucose tolerance in OGTT
5	Boerhaviadiffusa	Punarnava	Increase in hexokinase activity,decrease in glucose-6-phosphatase and fructose bis-phosphatase activity, increase plasma insulin level, antioxidant
6	Bombaxceiba	Semul	Hypoglycemic
7	Buteamonosperma	palasa	Antihyperglycemic
8	Camellia sinensis	Tea	Anti-hyperglycemic activity, antioxidant
9	Capparis decidua	Karir or Pinju	Hypoglycemic, antioxidant, hypolipidaemic
10	Caesalpiniabonducella	Sagarghota, Fevernut	Hypoglycemic, insulin secretagogue, hypolipidemic
11	Cocciniaindica	Bimb or Kanturi	Hypoglycemic
12	Emblicaofficinalis	Amla, Dhatriphala, a constituent of herbal formulation, “Triphala”	Decreases lipid peroxidation, antioxidant, hypoglycemic
13	Eugenia uniflora	Pitanga	Hypoglycemic, inhibits lipase activity
14	Enicostemalittorale	Krimihrita	Increase hexokinase activity, Decrease glucose 6-phosphatase and fructose 1,6bis-phosphatase activity. Dose dependent hypoglycemic activity
15	Ficusbengalenesis	Bur	Hypoglycemic, antioxidant
16	Gymnemasylvestre	Gudmar or Merasingi	Anti-hyperglycemic effect, hypolipidemic

17	Hemidesmusindicus	Anantamul	Anti snake venom activity, anti-inflammatory
17	Hibiscus rosa-sinesis	Gudhal or Jasson	Initiates insulin release from pancreatic beta cells
18	Ipomoea batatas	Sakkargand	Reduces insulin resistance
19	Momordicacymbalaria	Kadavanchi	Hypoglycemic, hypolipidemic
20	Murrayakoenigii	Curry patta	Hypoglycemic, increases glycogenesis and decreases gluconeogenesis and glycogenolysis
21	Musa sapientum	Banana	Antihyperglycemic, antioxidant
22	Phaseolus vulgaris	Hulga, white kidney bean	Hypoglycemic, hypolipidemic, inhibit alpha amylase activity, antioxidant. Altered level of insulin receptor and GLUT-4 mRNA in skeletal muscle
23	Punicagranatum	Anar	Antioxidant, anti-hyperglycemic effect
24	Salacia reticulate	Vairi	inhibitotory activity against sucrase, α-glucosidase inhibitor
25	Scopariadulcis	Sweet broomweed	Insulin-secretagogue activity, antihyperlipidemic, hypoglycemic, antioxidant
26	Swertiachirayita	Chirata	Stimulates insulin release from islets
27	Syzygiumalternifolium	Shahajire	Hypoglycemic and antihyperglycemic
28	Terminaliabelerica	Behada, a constituent of “Triphala”	Antibacterial, hypoglycemic
29	Terminaliachebula	Hirda	Antibacterial, hypoglycemic
30	Tinosporacrispa		Anti-hyperglycemic, stimulates insulin release from islets
31	Vincarosea	Sadabahar	Anti-hyperglycemic
32	Withaniasomnifera	Ashvagandha, winter cherry	Hypoglycemic, diuretic and hypocholesterolemic

INDIAN FORMULATED HERBAL DRUGS WITH ANTI-DIABETIC PROPERTIES

Drug	Company	Ingredients
Diabecon	Himalaya	Gymnemasylvestre, Pterocarpusmarsupium, Glycyrrhizaglabra, Casearіaesculenta, Syzygiumcumini, Asparagus racemosus, Boerhaviadiffusa, Sphaeranthusindicus, Tinosporacordifolia, Swertiachirata, Tribulusterrestris, Phyllanthusamarus, Gmelinaarborea, Gossypiumherbaceum, Berberisaristata, Aloe vera, Triphala, Commiphorawightii, shilajeet, Momordicacharantia, Piper nigrum, Ocimum sanctum, Abutilon indicum, Curcuma longa, Rumexmaritimus
Diasulin		Cassia auriculata, Cocciniaindica, Curcuma longa, Emblicaofficinalis, Gymnemasylvestre, Momordicacharantia, Scopariadulcis, Syzygiumcumini, Tinosporacordifolia, Trigonellafoenumgraecum
Pancreatic tonic 180 cp	ayurvedic herbal supplement	Pterocarpusmarsupium, Gymnemasylvestre, Momordicacharantia, Syzygiumcumini, Trigonellafoenumgraceum, Azadirachtaindica, Ficusracemosa, Aeglemarmelos, Cinnamomumtamala
Ayurveda alternative herbal formula to Diabetes:.	Chakrapani Ayurveda	Gurmar (Gymnemasylvestre) Karela (Momordicacharantia) Pushkarmool (Inularacemosa) JamunGutli (Syzygiumcumini) Neem (Azadirachtaindica) Methika (Trigonellafoenumgracecum) Guduchi (Tinosporacordifolia)
Bitter gourd Powder	Garry and Sun natural Remedies	Bitter gourd. (Momordicacharantia)
Dia-care	Admark Herbals Limited	SanjeevanMool; Himej, Jambubeej, Kadu, Namejav, Neemchal.
Diabetes-Daily Care	Nature’s Health Supply	Alpha Lipoic Acid, Cinnamon 4% Extract, Chromax, Vanadium, Fenugreek 50% extract, Gymnemasylvestre 25% extract Momordica 7% extract, Licorice Root 20% extract.

HERBOSOMES

Herbosomes are a current concept in herbal drug technology that removes the limitations of the traditional drug delivery systems and effectively used to enhance the bioavailability of many popular herbal extracts and phytoconstituents including Ginkgo biloba, milk thistle, grape seed, green tea, hawthorn, ginseng etc and can be developed for various therapeutic uses or dietary supplements. The herbosomal structures contain the active ingredients of the herb bounded to phospholipids. The molecular structure of phospholipid includes a water-soluble head and two fat-soluble tails. Because of this dual solubility, the phospholipid acts as an effective emulsifier.

This method can enhance the rate and the extent of drug absorption across the lipoid bio-membrane, which has been found promising for effective and appropriate systematic delivery of drug.

CONCLUSION

These medicinal plants provide a rich mine for bioactive constituents that are free from side effects and have powerful pharmacological actions. Diabetes mellitus is the one of the most leading disorders, which may increase the risk of secondary complications affecting the eyes, kidneys, nerves, heart, and arteries. Multiple of therapies are available for the treatment of diabetics. However, allopathic drugs are producing several unwanted side effects. It has been reported that anti-diabetic herbal medicines have a similar mechanism of action as allopathic drugs but negligible side effect with low cost. These plants have polyphenols, alkaloids, glycosides, polysaccharides, terpenoids, steroids, and flavonoids. These constituents are helpful in the treatment of many diseases including diabetics. By converting onto vesicular drug delivery system the bioavailability and permeation can be enhanced.

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