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Herbal Dietary Supplement

Ingredients Clinical Review

Management of the Diabetic Profile Using Indian Medicinal Plants – The Ayurveda

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Diabetes – extent of the global phenomenon and etiology. [1-3]:

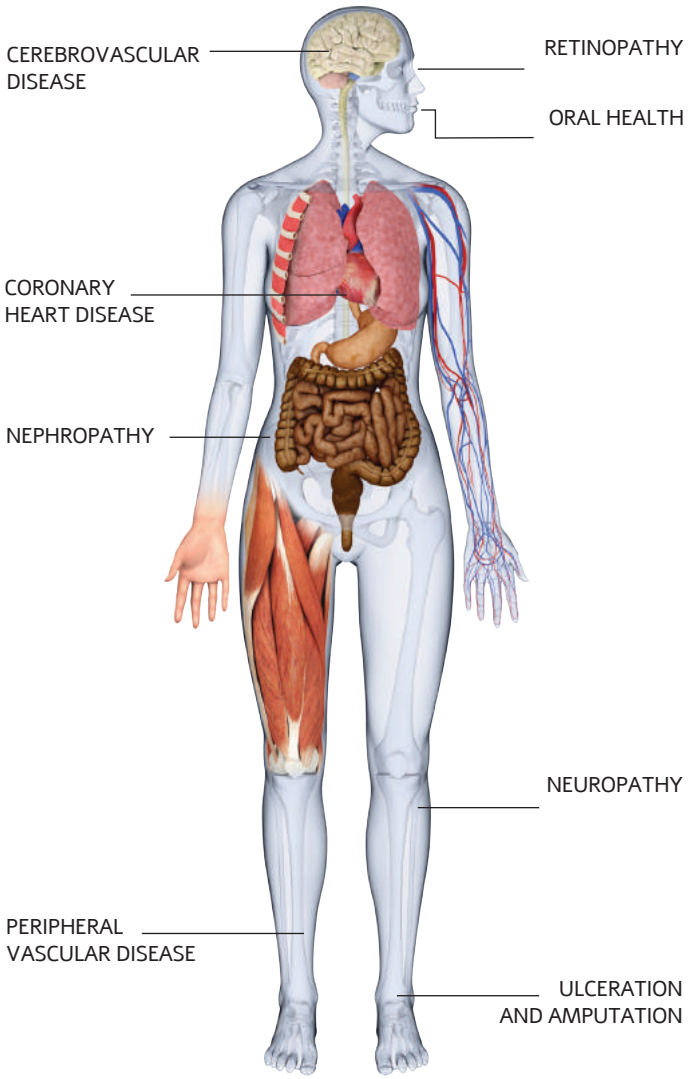
Diabetes Mellitus type II is also referred to as non-insulin dependent diabetes (NIDDM) has become a global epidemic. The morbidity rate in Western countries is estimated at over 10% of the general population (a phenomenon which is becoming widespread among children and adolescents as well).

What is glucose intolerance? How does diabetes develop and what are the possible complications?

The normal physiological mechanism of glucose absorption from the blood stream is mediated by the hormone insulin. This hormone is secreted as a response to carbohydrate intake, and is responsible for absorbing glucose by skeletal muscle and liver cells which store it as glycogen - an available glucose reserve between meals and during the overnight fast. During weight gain, the body attempts to cope with excess sugars in the blood by the secretion of an excess of insulin. Due to prolonged exposure of high levels of insulin, a decrease in sensitivity to insulin takes place (pre-diabetes) so that the amount of insulin secreted is no longer effective (insulin resistance). As a result, glucose levels in the blood start to rise and are often accompanied by an increase in blood lipid levels.

Prolonged exposure to high blood glucose levels harms how blood vessels function by the creation of free radicals and the development of sclerotic layers (the accumulation of blood lipids on blood vessel walls which block the cavities). Blood vessels potentially at risk include; coronary arteries (cardiac event); jugular veins (cerebral vascular accident – CVA); retinal blood vessels (blindness); the kidney (insufficiency); reproductive system (impotence); and nerve fibers (especially those responsible for sensations in the lower extremities).
An additional and significant impact of untreated diabetes is the appearance of "diabetic ulcers".

Diabetes Main Complications



Initial symptoms appearing at the onset of diabetes include: increased thirst and dry mouth, frequent urination (mainly at night) with a strong odor, fatigue from mild exertion (compared with previous activity), a feeling of intense hunger between meals coupled with a "drop" in the level of glucose between meals as shown by sweating, nervousness, a rapid pulse and blurriness. There is great importance in diagnosing the disease in its early stages (the time when there is a decrease in tolerance to insulin), to treat it when it appears and for continuous management among chronic patients.
A decrease in the amount of insulin secreted is seen with the advancement of the disease and at this stage, it is customary to combine treatment with exogenous insulin.

Most conventional medicines given orally are usually accompanied by side-effects and those given by injection have low patient compliance to treatments.

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Dietary supplement – Herbal blend

Indian medicinal plants recruited in the treatment of diabetes - treatment characteristics clinically investigated.
Indian medicine using plants (the Ayurveda) uses the accumulated botanical knowledge of plants whose actions and unique medical properties have been used over thousands of years of practical treatment.
The nutritional supplement from CuraLife takes plants known and used in traditional medicine for the treatment of diabetes. The plants grow in a mineral rich environment and together with the extraction of the active ingredients by a unique method, and combination of active ingredients for optimal synergy provide a formula that achieves maximal effect.

The plants and their unique characteristics are detailed below

1 Momordica Charantia

Also known as "Bitter Melon" grows in tropical areas such as the Far East, the Caribbean and East Africa. In Asia, the fruit is traditionally used as a nutritional ingredient to treat diabetes, mainly in its early stages (insulin intolerance) and also to lower blood lipid levels. Among the active ingredients are vicine, charantin, triterpenoids and anti-oxidants which reduce the level of free radicals[4]. Their impact includes the regeneration of the physiological function of damaged pancreatic cells and improvement of their efficiency[5], reduction of glucose absorption from the intestine, increase in muscle cell sensitivity to insulin and the reduction of gluconeogenesis activity (which converts glucose reserves in the liver to available glucose)[6].

A study examined the effect of the substance on 42 Taiwanese men and women with a mean age of 45.7 + 11.4, who displayed at least three symptoms of metabolic syndrome - hypertension, hyperlipidemia, abdominal obesity and insulin resistance - which constitute early symptoms of the development of diabetes. The study demonstrated a statistically significant decrease ($p=0.021$) of 19% in the labeled cases of the syndrome (after only three months of treatment) and a mean decrease in waist circumference at a mean rate of approximately 2 cm. The continuous effect of treatment was maintained for an additional month after the end of taking the supplement[7].

In 2011, a study lasting approximately four weeks was published[8] that compared the conventional drug treatment metformin (at a dosage of 1,000 mg) and the use of 2,000 mg of the fruit extract. In both cases, the treatments demonstrated a decrease in the level of the glucose indicator fructoseamine, while the rate of decline was higher among those taking metformin. However, it should be noted, the side-effects of metformin sometimes reduce patient compliance.

A further trial performed on rodents demonstrated a significant statistical increase in the number of glucose transporters in muscle cells (Glut4), responsible for the uptake of glucose from the bloodstream, and an increase in the expression of peroxisome proliferator-activated receptor γ enzymes in adipose and muscle cells. These enzymes are responsible for the decrease in insulin resistance in the above mentioned tissues[9]. Of note is that the activity of PPAR γ constituted a central target for a very efficient prescription drug (Rosiglitazone) which was taken out of use a number of years ago due to a problematic safety profile for which an alternative has recently been re-introduced.

2 Gymnema Sylvestre

Gymenema is known for its ability to decrease the craving for the characteristic sweet taste of carbohydrates. The active substance saponin connects to receptors for the sweet taste found on the tongue and prevents their activity, thereby lowering the strong craving for sweet foods. From the metabolic perspective, the substance hastens the release of insulin from the pancreatic cells, slows the absorption rate of carbohydrates from the digestive system, which contributes to the feeling of satiety for a longer period of time and indirectly to weight loss.

Additional active substances include gymnemic acid, stigmasterol, quercitol, choline, triethylamine and derivatives of the amino acid betaine[10]. A number of studies[11-12] conducted to examine the efficacy of Gymenema in continued treatment demonstrate a decrease in glucose to normal level values, without cases of hypoglycemia (the sharp decline in blood glucose levels needed for normal nerve activity which can stimulate reactions such as nervousness, tremors, a rapid pulse, sweating, blurriness and can even be life threatening).

A study published in 2001 examined how continuous daily consumption (90 days) of the substance affected the fasting blood glucose level; glucose measured two hours after a meal and the level of HbA1c. The study included 65 diabetics, and demonstrated a statistically significant mean decrease at a rate of 11%, 13% and 0.6% respectively in each of the measures[13].

A pioneering study on the subject, conducted in India in 1990 included 22 volunteers. Aged 40-62 they had been diagnosed with the disease for duration of between 1-12 years and had used the substance for a period of 18-20 months. A mean decrease of approximately 28% was seen in fasting blood glucose levels, and 21 volunteers reduced the levels of conventional drug treatment with five volunteers stopping altogether. A control group without the supplement was followed during this period and the level of conventional treatment increased due to the rise in fasting glucose[14].

3 Trigonella Foenum-Graecum

Also known as Fenugreek contains a high amount of fiber and alkaloids, which improve the ability of the pancreas to produce and release insulin mainly due to the presence of the amino acid 4-hydroxylisoleucine which regulates the release rate of insulin, so it is compatible with blood glucose levels.

Fenugreek seeds have also been attributed with the property of slowing down the absorption rate of carbohydrates from the digestive system.
A study published in 2001 included 25 people recently diagnosed diabetics. This group was divided into two sub-groups. The first included 12 people who received daily treatment for a period of two months while a second group of 13 people received a placebo. Results of the study did not find a significant difference in either the fasting blood glucose level or in glucose levels two hours after a meal, but did demonstrate a lower level of plasmatic glucose over time (calculation of the area under the curve which describes daily accumulating levels) and higher levels of insulin secreted which was statistically significant ($p<0.001$)[15].

4 Curcuma Longa

Turmeric is known for its culinary properties and has been used for thousands of years in Indian and Chinese medicine for the treatment of diabetes. The active substance in turmeric, curcumin, is known for its ability to reduce Glucose levels and treat complications of diabetes[16].

The active mechanism of the substance is linked to its ability to moderate immune activity, that is, reduce the level of substances secreted from the immune system (NFk-B, TNF). These substances are also responsible, for raising insulin resistance. Another property includes raising sensitivity to insulin by the enzymatic activity of PPAR γ in muscle cells and fat[16-17].

A double-blind study published in 2012 took a group of 120 identified as pre-diabetics and examined how prolonged exposure to this supplement (9 months) might affect the rate at which the subjects condition deteriorated to diabetes. Parallel control group received a placebo throughout the duration of this period. In the group receiving the supplement, there was no event of deterioration occurring, while in the control group, over 16% were diagnosed as diabetic with lower levels of insulin secretion and high resistance to insulin[17].

5 Emblica Officinalis

The active ingredient in the plant is tannoid whose properties work to restore the function of pancreatic cells. A study from 2012 examined 42 mice in which type-II diabetes was induced (by way of pharmacological treatment). The mice were divided into seven groups, where each group was given the plant in various doses for a period of 45 days. Afterwards, the plasmatic glucose level and insulin level were examined and a significant statistical increase was found to be dependent on the dose amount. A histological change in the pancreatic tissue which demonstrated its restoration was also observed[18].

A study published in 2009, examined in a similar model tested on mice, saw a decrease in fasting glucose levels three hours after the glucose loading test. For mice who were treated with the plant, a decrease was observed of 25% and 41.6% respectively for each of the measures[19].

6 Swertia Chirata

This plant grows mainly in the Himalayas and contains a number of active ingredients including chirtin, ophelic acid and mangiferin.

Their properties include the direct activation of pancreatic cells to release insulin, the reduction of glucose absorption from the digestive system, improvement of the break-down process of cellular glucose (process of glycolysis) and an increase in the peripheral use of glucose by skeletal muscles and its storage in the liver and muscles.

In addition (and similarly to new prescription drugs), it raises the activity of the enzyme dipeptidyl peptidase IV (DPP4) and levels of the glycogen-like peptide GLP1. The hormone GLP1 (also called incretin) is released from the intestinal cells as a physiological reaction to the increase in the levels of absorbed glucose and regulates the secretion of insulin from the pancreas. In addition, GLP1 inhibits the breakdown of glycogen reserves in the body, contributes to the feeling of satiety by inhibiting gastric emptying and "signals" to the center of satiety in the hypothalamus. The enzyme DPP4 inhibits the evacuation rate of incretins, for example GLP1, and indirectly prolongs its effect[20].
A study published in 2007 observed 48 mice that were divided into three groups, within which there was a control group of six mice and a study group.

The study groups were fasting mice, mice which now were balanced and diabetic mice. The plant extract was administered and glucose measurements were examined at different time periods: immediately, after one hour, three hours and four hours. In the healthy group which was recently balanced and the diabetic group, there was a significant decrease after three hours at a rate of over 13% and over 30% respectively. No incidents of hypoglycemia appeared among fasting mice, a result supporting treatment safety[21].

A further study[22] published in 2013 in which 24 mice were divided into four groups: a control group that received saline for a period of 21 days, and in the additional three groups, type-II diabetes was induced by drug treatment as part of a model common in the study of mice. Out of the three diabetic groups, the first group did not receive treatment but only saline, the second received an extract from the plant and the third received drug treatment with the substance Glibenclamide, a common prescription drug, which stimulates the secretion of insulin from the pancreas. Blood glucose levels were measured at the start of the trial, after 3 days, 7 days, 14 days and 3 months.
The results demonstrated a significant decrease in the level of glucose just three days after taking it, an effect which reached its peak after 14 days (values which are not significantly different from glucose values in the control group). The decrease observed was lower than the decrease in glucose levels as a result of the drug treatment. However, it should be remembered that the prescription drug is not without side-effects, for example hypoglycemia and so the extract operates with a greater safety range.

7 Picrorhiza Kurroa

Animal model (rats) of severe diabetes type 2 was investigated. The rats were exposed to Picrorhiza kurroa extract for 14 days whereas another group received the conventional therapy with glibenclamide.

The result indicated a significant reduction in average±standard deviation of fasting blood glucose levels from 345.83 ±25.93 to 94.01±4.98 mg/dL. A similar tendency was found in the glibenclamide group-a decrease from average value of 300.84± 21.99) to 88.77 ±2.53 mg/dL[23].

8 Syzygium Cumini
Eugenia Jambolana

The hypoglycaemic effect of E. jambolana was investigated in diabetic rabbits.

Hypoglycaemic activity was assessed by reduction in fasting blood glucose (FBG) and also in peak blood glucose during glucose tolerance test (GTT) in sub-diabetic and mild diabetic (MD) rabbits, but in severe diabetic (SD) rabbits by reduction in The extract when given orally to sub-diabetic (AR) for 1 day, MD for 7 days and SD for 15 days showed significant fall in FBG (12% AR, 18.9% MD and 29% SD) and also produced 16.9% fall in peak blood glucose in AR and 21% in MD rabbits during GTT. When administered daily for 15 days to MD and SD rabbits, significant fall in FBG (41.3% MD, 31.6% SD) and glycosylated haemoglobin (GHb) levels (23.3% MD, 26.6% SD) were observed, while serum insulin level showed significant increase (32.8% MD, 26.9% SD). Liver and muscle glycogen content also increased[24].

Another animal study using rats model of diabetes type 2 exposed to 15 days of Eugenia Jambolana. A statistically significant ($p<0.001$) decrease in blood fasting glucose was obtained in the intervention group in comparison to the diabetic control group (average value ± standard deviation): 75±11.9 vs 123±14.4 mg/dL, respectively)[25].

9 Tinospora Cordifolia

In this study, the chronic (100 days) antihyperglycemic effect of the extract was investigated. Fasting blood glucose, glycosylated hemoglobin (HBA1C) and serum insulin levels were evaluated in normal, diabetic and treated rats.

The extract significantly reduces the fasting blood glucose level, glycosylated hemoglobin level as compare to diabetic control ($p<0.001$), the insulin and C-peptide levels were improved which shows the regeneration of β-cell which secretes insulin[26].

Another research that exposed the rats to Oral treatment of for 14 days regulated blood glucose, provoked insulin secretion and also suppressed oxidative stress marker, formation and restored cellular defense anti-oxidant markers in the liver. Treatment with also inhibited glucose 6-phosphatase and fructose 1,6-diphosphatase ($p < 0.001$); and restored glycogen content in liver ($p < 0.005$)[27].

In conclusion, the traditional plant Tinospora cordifolia mediates its anti-diabetic potential through mitigating oxidative stress, promoting insulin secretion and also by inhibiting gluconeo- genesis and glycogenolysis, thereby regulating blood glucose.

10 Melia Azadirachta

A study was designed to investigate clinically the hypoglycemic effect of seeds of Azadirachta indica in Type-2 diabetes mellitus.

After assaying fasting plasma and urinary glucose, 10 patients with type-2 diabetes mellitus with no previous medication, 10 patients with type-2 diabetes mellitus taking oral hypoglycemic agents with history of inadequate control and six control subjects were given low and high doses of powdered extract of Azadirachta indica for 14 days. On the 15th day, blood and urine samples for glucose were taken. Based on results obtained it was found that Azadirachta indica has significant hypoglycemic activity in high dose and can be successfully combined with oral hypoglycemic agents in type-2 diabetic patients whose diabetes is not controlled by these agents[28].

Another human study compared fasting glucose level in both diabetic control group and intervention group which was exposed to Azadirachta extract for two months. The group showed a statistical significant reduction in blood fasting glucose was obtained (125±12 to 120±9 mg/dl, $p<0.03$)[29].

SUMMARY

Synergistic treatment combines various active functions to improve the efficacy of medical treatment. In this instance, this is used to achieve a common goal – the balance and reduction of glucose levels during fasting and after eating.

The combination of active functions include: inhibiting the absorption and breakdown of sugars in the intestine to prolong the feeling of satiety (which contributes over time to weight-loss), a reduction in the breakdown rate of glucose reserves in the liver between meals (a characteristic of diabetics), restoration of pancreatic cells' ability to secrete insulin and control of its rate of secretion, so that it is compatible with the plasma glucose levels.

Moderate immune activity reduces the level of hormone tissue responsible for the increase of insulin resistance; increasing receptor activity in the PPAR γ receptor cells in adipose tissue, responsible for the reduction of insulin resistance and an increase in the level of glucose carriers in muscle cells.

The increase in the levels of the enzyme DPP4 and the levels of the hormone GLP1 improves the normal physiological function of insulin secretion, an activity thought to be the objective of most advanced drug treatments, is also found in these traditional plant remedies.

*** Comment:**
The medical information published in this review should not be seen as a substitute for treatment or conventional medical advice. Children, pregnant or lactating women should not take the supplement. Those suffering from hypoglycemia and children under the age of 18 should not take the supplement. Patients with chronic illnesses taking medication should consult their treating physician before starting to use the nutritional supplement. Diabetic patients receiving drug treatment should monitor blood glucose levels at the start of use of the nutritional supplement in order to prevent cases of hypoglycemia.

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