Ingredients Literature Review

for ayurvedic glucose support formulations

Ingredients and their unique characteristics

1 MOMORDICA CHARANTIA

Also known as bitter melon, this member of the squash family 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 resistance). It is also used to lower blood lipid levels. Among its active ingredients are vicine, charantin, triterpenoids, and antioxidants that reduce free radical levels.[4] Benefits include regeneration of the function of damaged pancreatic cells and improvement of their efficiency, reduction of glucose absorption from the intestine, increased muscle cell sensitivity to insulin, and reduction of gluconeogenesis activity (which converts glucose reserves in the liver to available glucose).[5]

A study examined the effect of the plant on 42 Taiwanese men and women (mean age 45.7 ± 11.4) who displayed at least three symptoms of metabolic syndrome (the early symptoms of diabetes): hypertension, hyperlipidemia, abdominal obesity, and insulin resistance. The study demonstrated a statistically significant decrease ($p = 0.021$) of 19% in the cases of metabolic syndrome after three months, and a mean decrease in waist circumference of approximately 2 cm. The effects of treatment were maintained for an additional month after discontinuing the supplement.[7]

A 2011 study compared the conventional drug metformin (at a dosage of 1,000 mg) and the use of 2,000 mg of bitter melon extract over a period of approximately four weeks. Both treatments decreased the level of the glucose indicator fructosamine, while the rate of decline was higher among those taking metformin. It should be noted, however, that the side effects of metformin sometimes reduced patient adherence.

A 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] Additionally, the activity of PPAR γ constituted a central target for a very efficient prescription drug (Rosiglitazone) that saw a decline in use a number of years ago due to a problematic safety profile.

2 GYMNEMA SYLVESTRE

Gymnema sylvestre 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 conducted to examine the efficacy of Gymnema 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).[11-12]

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, the volunteers had been diagnosed with the disease for a duration of 1-12 years and used the substance for a period of 18-20 months. A mean decrease of approximately 28% was seen in fasting blood glucose levels. 21 volunteers reduced their levels of conventional drug treatment with five volunteers fully stopping. A control group was followed during this period and the level of conventional treatment increased due to the rise in fasting glucose.[14]

EMBELICA OFFICINALIS 3

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 and insulin levels 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]

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]

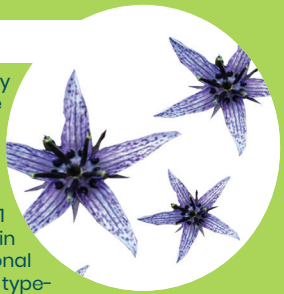
The active mechanism of the substance is linked to its ability to moderate immune activity and reduce the level of substances secreted from the immune system (NFk-B, TNF). These substances are responsible for raising insulin resistance. Another property includes raising sensitivity to insulin by the enzymatic activity of PPAR γ in muscle cells and fat.[16-17] A double-blind study published in 2012 took a group of 120 people 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. The 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]

TRIGONELLA FOENUM GRAECUM 5

Also known as Fenugreek, Trigonella Foenum Graecum 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.

When ingested, Fenugreek seeds are able to slow down the absorption rate of carbohydrates from the digestive system. A study published in 2001 included 25 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 the 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 statistically signifcant higher levels of insulin secreted ($p<0.001$).[15]

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 each group 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]

In a 2013 study 24 mice were divided into four groups: a control group that received saline for 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.[22] Out of the three diabetic groups, the first group did not receive treatment (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 has side-effects, for example hypoglycemia and so the extract operates with a greater safety range.

7 SYZYGIUM CUMINI | EUGENIA JAMBOLANA

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

Hypoglycemic 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. In severe diabetic (SD) rabbits when E. jambolana was given orally to sub-diabetic (AR) for 1 day, MD for 7 days, and SD for 15 days, a significant fall in FBG (12% AR, 18.9% MD and 29% SD) was observed. It also produced a 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, a significant fall in FBG (41.3% MD, 31.6% SD) and glycosylated hemoglobin (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 were 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]

8 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 compared to the 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 study that exposed the rats to oral treatment for 14 days regulated blood glucose, provoked insulin secretion, suppressed oxidative stress marker, and restored cellular defense anti-oxidant markers in the liver. Treatment also inhibited glucose 6-phosphatase and fructose 1,6-diphosphatase ($p < 0.001$); and also 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 gluconeogenesis and glycogenolysis, thereby regulating blood glucose.

9 MELIA AZADIRACHTA

Melia Azadirachta, also referred to as Azadirachta indica and as Indian lilac, is known in Ayurveda for its anti-diabetic properties. It is a rich source of antioxidant and scientific research has identified hundreds of active compounds from various parts of the plant which support many cardiovascular conditions.

A study was designed to clinically investigate 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 histories 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 has significant hypoglycemic activity in high doses 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 (125±12 to 120±9 mg/dl, $p<0.03$).[29]

10 PICRORHIZA KURROA

Picrorhiza Kurroa, also known at Kutki, is found in the Himalayan region. The rhizome has a long history of use in Indian Ayurvedic medicine. It has hepato-protective properties and thus supports the healthy processes managed in the liver and spleen. The chemical composition of Picrorhiza Kurroa includes Kutki and Kutakoside. An animal model of severe type 2 diabetes was investiaged using rats. They were exposed to Picrorhiza kurroa extract for 14 days. Another group received conventional therapy with glibenclamide. The results showed 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 an average value of 300.8 ± 21.99 to 88.77 ± 2.53 mg/dL.

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