

MULTI-HERBAL MEDICINAL COMPOSITE FOR TREATING THE
METABOLIC SYNDROME AND PREPARATION METHOD THEREOF

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention relates to a multi-herbal medicinal composite and a preparation method thereof, and particularly to specific a multi-herbal medicinal composite for treating the metabolic syndrome and a preparation method thereof.

Description of the Related Art

The metabolic syndrome is a combination of medical disorders that increase the risk of developing cardiovascular disorders and diabetes. The risk factors include the following abnormalities: 1) abdominal obesity (excessive fat tissue in and around the abdomen); 2) atherogenic dyslipidemia (blood fat disorders — high triglycerides, low HDL cholesterol and high LDL cholesterol — that foster plaque buildups in artery walls); 3) elevated blood pressure; 4) insulin resistance or glucose intolerance (the body can't properly use insulin or blood sugar); 5) prothrombotic state (e.g., high fibrinogen or plasminogen activator inhibitor-1 in the blood); and 6) proinflammatory state (e.g., elevated C-reactive protein in the blood).

Diabetes mellitus resulting from various risk factors, such as high fasting blood glucose, impaired glucose tolerance, or insulin resistance, can become life-threatening chronic disorders. At present, the metabolic syndrome is defined by the following conditions, and presence of any three or more the following conditions.

Five Major Risk Factors	Abnormal Standards
Central Obesity	Waist Circumference Male : $\geq 90\text{cm}$; Female : $\geq 80\text{cm}$
Elevated Blood Pressure (BP)	SBP $\geq 130\text{mmHg}$ DBP $\geq 85\text{mmHg}$
Reduced High Density Lipoprotein - Cholesterol (HDL-C)	Male : $\leq 40\text{mg/dL}$ Female : $\leq 50\text{mg/dL}$
Elevated Fasting Glucose	FG $\geq 100\text{mg/dL}$
Elevated Triglycerides	TG $\geq 150\text{mg/dL}$

Insulin Resistance (Metabolic Syndrome)	Diabetes				
					
Increased body weight	Increased body weight	Increased body weight	Decreased body weight	Death	
Increased insulin secretion	Increased insulin secretion	Insulin secretion reaches a relative climax	Decreased insulin secretion		
Insulin resistance	Insulin resistance	Insulin resistance	Blood glucose reaches a relative climax		
Normal blood glucose	High blood glucose	Rapidly elevated blood glucose	Pancreas β -islet cell atrophy starts		
(1)	(2)	(3)	(4)		

(Development process from the metabolic syndrome to diabetes)

Regular exercise regimens, good dietary habits and regular medical check-ups are good way for preventing the metabolic syndrome. Currently, when diabetes is diagnosed, choices of secretagogues drugs such as sulfonylurea and meglitinides, sensitizers such as biguanides and thiazolidinediones biguanides, and alpha-glucosidase inhibitors are administered. Insulin injection is also a treatment choice for diabetes.

Recently, ample scientific evidence strongly shows that some herbal extracts have hypoglycemic effects. However, the pharmacological and clinical evidence for treating hyperglycemia are still limited. In addition, the evidence of herbal-based products for treating hyperglycemia is yet convincing. Not only the effectiveness of the herbal-based products is generally weaker than synthetic anti-diabetic medications, but also the pharmacological mechanisms are uncertain.

It is noteworthy to point out that most products, which comprise drugs or supplements, for treating hyperglycemia are via a single pharmacological mechanism. The common choices include secretagogues, insulin sensitizer and alpha-glucosidase inhibitor administered to control blood glucose by a single action, and the pharmacological actions are either to enhance secretion of insulin or reduce insulin resistance. However, the cause of glucose metabolism disorder is two-fold: 1) the progression of diabetes normally starts with insulin resistance followed by 2) hyperinsulinism which will later result in impairment of insulin secretion due to β -cell dysfunction (atrophy). A single mechanism approach to treat such disorder seems insufficient, especially not

knowing the pathological status of the patient. Nevertheless, correcting insulin resistance is a key to improve or to prevent diabetes from occurring. Combining other correcting factor such as secretagogues will be more effective to correct the possible underlying pathological causes.

SUMMARY OF THE INVENTION

In view of the foregoing shortcomings of the prior art, the inventor of the present invention successfully developed a multi-herbal medicinal composite for treating the metabolic syndrome, and the primary ingredients of the multi-herbal composite are *bidens pilosa* and *panax ginseng*. As indicated in references, both *bidens pilosa* and *panax ginseng* have the effects of lowering the level of blood glucose with distinct mechanisms. *Bidens pilosa* can be used as insulin secretagogues which can help insulin secretion of pancreatic β -cell. On the other hand, *panax ginseng* can be used as insulin sensitizer to improve insulin sensitivity for metabolizing glucose in the peripheral tissues. Therefore, the present invention combines *bidens pilosa* and *panax ginseng* in a proprietary proportion to achieve the effects of promoting insulin secretion and reducing insulin resistance, and to counterbalance their medicinal shortfalls. The present invention is also suitable for individuals with different physique natures.

The primary objective of the present invention is to provide a multi-herbal medicinal composite to treat the metabolic syndrome.

To achieve the foregoing objective, the present invention provides a multi-herbal medicinal composite comprising *bidens pilosa* and *panax ginseng* to treat metabolic syndrome. The composite comprises 65 wt%~95 wt%, preferably 80 wt%, of *bidens pilosa* and 5 wt%~35 wt%, preferably 20 wt%, of *panax ginseng*.

The multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention comprises *bidens pilosa* and *panax ginseng* to promote insulin secretion and reduce insulin resistance. Thus, the multi-herbal medicinal composite is capable of regulating the blood glucose level and thus suitable for treating diabetic patients.

The present invention provides a preparation method of the multi-herbal medicinal composite for treating the metabolic syndrome, and the method comprises the steps of: (a) mixing *bidens pilosa* and *panax ginseng* according to the respective weight percentage given in claim 1 to form a main raw material; (b) extracting the main raw material by an appropriate solvent to obtain an extract liquid; (c) filtering the extract liquid and then concentrating the filtered extract liquid; and (d) drying the concentrated extract.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 shows results of fasting glucose levels of diabetic mice with long-term treatment;

FIG. 2 shows results of postprandial blood glucose levels of diabetic mice with short-term treatment;

FIG. 3 shows results of oral glucose tolerance of diabetic mice with short-term treatment;

FIG. 4 shows results of fasting glucose levels of diabetic mice with short-term treatment;

FIG. 5 shows results of postprandial blood glucose levels of diabetic mice

with short-term treatment;

FIG. 6 shows results of oral glucose tolerance of diabetic mice with long-term treatment;

FIG. 7 shows results of fasting glucose levels of diabetic mice with long-term treatment;

FIG. 8 shows results of blood insulin levels of diabetic mice with short-term treatment;

FIG. 9 shows the changes of fasting glucoses levels of diabetic patients before and after taking MetaJust for one to three months; and

FIG. 10 shows the changes of glycosylated hemoglobin (HbA1c) of diabetic patients before and after taking MetaJust for three to six months.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The invention relates to a multi-herbal medicinal composite for treating the metabolic syndrome, and the multi-herbal medicinal composite comprises 65%~95% preferably 80% (by weight) *bidens pilosa* and 5%~35% preferably 20% (by weight) *panax ginseng*. The properties of each ingredient are listed below:

1. *Bidens pilosa*

Bidens pilosa is a species in the plant family *Asteraceae*, and the common ones include *B. pilosa* var. *radiata*, *B. pilosa* var. *minor*, *B. pilosa* var. *pilosa* and *B. pilosa* var. *bisetosa*. In reference, *bidens pilosa* comprises many secondary metabolites with different chemical structures, including the flavonoids, phenoxypropionic acids and polyacetylenes, etc, for being used as a health

supplement herbal tea. *Bidens pilosa* has the functions of detoxification, urination and blood circulation activation, as well as curing gastro-intestinal diseases, infections and inflammation. According to scientific references and research discoveries, *bidens pilosa* is found extensively in continents including Africa, America and Asia and is used for curing inflammations and diabetes mellitus. A whole plant of *B. pilosa* var. *radiata* can be used for treating diabetes mellitus induced by Alloxan. In addition, the n-butyl alcohol extract of the *B. pilosa* var. *radiata* is proved to have the function of regulating our immune system to prevent Type 1 diabetes mellitus (Autoimmune diabetes mellitus).

As to the study of the functions and mechanisms of *bidens pilosa* in treating diabetes, it is suggested to have the abilities enhancing insulin secretion and synthesis in pancreas β -islet cells. The specific extracts, polyacetylene compounds, of *bidens pilosa* also show the ability of lowering the of blood glucose level in the cases of hyperglycemia. It is noteworthy to point out that methanol extracts and polyacetylene extracts of *bidens pilosa* have the functions of lowering blood glucose level in Type 2 diabetic mice.

2. *Panax ginseng*

Compound K (CK) in *Panax ginseng* is capable of elevating the level of adiponectin in blood plasma and activating genes of lipogenesis and glucose transporters, and thus increases the level of insulin reaction. Besides CK, ginsenoside-RH2 is also proved to be able to regulate blood glucose level by increasing the sensitivity to insulin.

For simplicity, the multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention makes use of

compounds in the bidens pilosa such as the cytopiloynes produced by Aggie Bionatural Technology to promote insulin secretion as well as synthesis, and also make use of the ginoside in panax ginseng to increase the sensitivity to insulin, so as to achieve the effect of treating metabolic syndrome.

The multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention has the functions of regulating the blood glucose level and are applicable to cure diabetes mellitus.

The multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention has the function of promoting insulin secretion and synthesis.

The multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention has the function of reducing insulin resistance.

The multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention is in the form of a tablet, grain, powder, liquid, capsule or honeyed pill, etc and can be added into drinks, meals, or other food products.

In addition, in the multi-herbal medicinal composite for treating the metabolic syndrome in accordance with the present invention, bidens pilosa and panax ginseng are in the form of an extract, preferably in the form of an aqueous extract.

Description of Examples of Tests

The present invention is illustrated in details by the following embodiments, but the scope of our invention is not limited to the embodiments described below.

Preparation of Multi-Herbal Medicinal Composite (MetaJust)

In the present invention, the whole plants of *Bidens pilosa* can be used and are not limited to any particular place of origin, and *Panax ginseng* is not limited to any particular portion of plant or any particular place of origin.

Preferably, *Bidens pilosa* is used with the leaf and stem portion of a plant whose height is 60~150 cm, and the plant is a non-flowering one. The place of origin is preferably a sub-tropical zone, and the harvest seasons are preferably summer and autumn. Fresh or dried plants can be used after the harvest, but the dried method should not be too long during the time exposed to the sun. In order to increase extraction yield, the dried plant requires grinding into powder.

Preferably, *Panax ginseng* is used from Korean red ginseng with age over 4 years, and the dried ginseng requires grinding into powder as used.

Firstly, the two herbal medicines are dried and ground into powder, and then extracted with hot water after mixing two kinds of powder. The extraction process is carried out for three times. The first extraction is that 500~1000 L of filtered pure water is added into 30~50 kg of main raw material, wherein the volume of pure water is 20~40 times of main raw material, and then is heated at 80~100 °C for 30~50 minutes, and finally the filtered liquid is concentrated. Similarly, the second extraction is that 500~1000L of filtered pure water is added into the main raw material, wherein the volume of pure

water is 20~40 times of main raw material, and then is heated at 80~100 °C for 40~70 minutes, and finally the filtered liquid is concentrated. Similarly, the third extraction is that 500~1000L of filtered pure water is added into the main raw material, wherein the volume of pure water is 20~40 times of main raw material, and then is heated at 80~100 °C for 40~70 minutes, and finally the filtered liquid is concentrated. The concentrated liquid is collected and concentrated to a concentration of 30~60% and then turned into powder by spraying or freeze drying, and the dried powder is mixed according to the aforementioned proportion to form an excipient, and finally the multi-herbal medicinal composite (MetaJust) in accordance with the present invention is produced.

Comparison between Multi-Herbal Medicinal Composite (MetaJust) and

Bidens pilosa (BP)

To demonstrate the difference of effects for the multi-herbal medicinal composite (MetaJust) and recipe of *B. pilosa* var. *radiata* (BP) to control blood glucose of diabetic patients, two experiments are conducted, wherein the first part is long-term fasting glucose levels and the second part is short-term postprandial blood glucose levels. Certified Type 2 diabetic mice (db/db mice) are used and divided into three groups: the first group includes the same quantity vehicle treatment to diabetic mice as a control group, and the second and the third group include *Bidens pilosa* (BP) and MetaJust treatment to diabetic mice as experimental groups.

With reference to FIG. 1 for the results of fasting glucose levels during long-term treatment to diabetic mice, the results show that there is significant decrease of the blood glucose value for both BP and MetaJust compared with

the control group on the 7th day. Specifically, only treatment of MetaJust on the 14th day is under control, and it indicates the superior effect of treatment of MetaJust compared with BP during long-term levels.

With reference to FIG. 2 for the results of postprandial blood glucose levels during short-term treatment to diabetic mice, the results show that there is similar effect of lower blood glucose value for both BP and MetaJust. It indicates the same effect of treatment of BP and MetaJust during short-term levels.

Animal Experiment Data of Multi-Herbal Medicinal Composite (MetaJust)

According to varied methods of the blood glucose test, we can observe changes of the blood glucose value for treatment of MetaJust to Type 2 diabetic mice (db/db mice), and the experiment contents comprise short-term oral glucose tolerance levels, short-term fasting glucose levels, short-term postprandial blood glucose levels, long-term oral glucose tolerance levels, and long-term fasting glucose levels. In addition, we can observe changes of the blood insulin value for short-term treatment of MetaJust to diabetic mice.

Certified Type 2 diabetic mice (db/db mice) are used as blood glucose test. The experiments are conducted and divided into two groups, wherein one group is for the same quantity vehicle treatment to diabetic mice as a control group, and the other group is for treatment of MetaJust to diabetic mice as an experimental group.

For oral glucose resistance levels during short-term treatment to diabetic mice, the diabetic mice fed with glucose (1g/kg) after fasting overnight, and then fed with vehicle and MetaJust respectively after 30 minutes. With reference to FIG. 3 for the results of oral glucose tolerance levels during

short-term treatment to diabetic mice, the results show that there is a significant decrease for the blood glucose value of MetaJust treated group compared with the control group during short-term levels.

For fasting glucose levels during short-term treatment to diabetic mice, with reference to FIG. 4 for the results of fasting glucose levels during short-term treatment to diabetic mice, the results show that there is a lower blood glucose value for MetaJust treated group compared with the control group during short-term levels.

For postprandial blood glucose levels during short-term treatment to diabetic mice, the diabetic mice fed with glucose (1g/kg) after fasting overnight, and then fed with vehicle and MetaJust respectively after an hour. With reference to FIG. 5 for the results of postprandial blood glucose levels during short-term treatment to diabetic mice, the results show that there is a significant decrease for the blood glucose value of MetaJust treated group compared with the control group during short-term levels.

For oral glucose tolerance levels during long-term treatment to diabetic mice, with reference to FIG. 6 for the results of oral glucose tolerance levels during long-term treatment to diabetic mice, the results show that there is a lower blood glucose value for MetaJust treated group compared with the control group after 32 days during long-term levels.

For fasting glucose levels during long-term treatment to diabetic mice, with reference to FIG. 7 for the results of fasting glucose levels during long-term treatment to diabetic mice, the results show that there is a significant decrease for the blood glucose value of MetaJust treated group compared with the control group after 32 days during long-term levels.

For blood insulin levels during short-term treatment to diabetic mice, the diabetic mice fed with glucose (1g/kg) after fasting overnight, and then fed with vehicle and MetaJust respectively after 30 minutes. With reference to FIG. 8 for the results of blood insulin levels during short-term treatment to diabetic mice, a pre-dose group is defined as a blood insulin value without the dosage of glucose to diabetic mice of overnight fasting. The control and MetaJust groups are defined as blood insulin values with vehicle and MetaJust respectively after 30 minutes for the dosage of glucose to diabetic mice of overnight fasting. The results show that there is a significant effect of the higher blood insulin value for MetaJust treated group compared with the pre-dose and control groups during short-term levels.

As mentioned previously, the references are illustrated with the effect and principle of dosage of our invention (MetaJust) to diabetic disorder, and there is no intent to limit it to those embodiments. On the contrary, modification of aforesaid references is complied with the essence of our invention (MetaJust), but it is against the scope of claims as following our patent.

Clinical Experiment Data of Multi-Herbal Medicinal Composite (MetaJust)

As the dosage of MetaJust to diabetic patients who is poor control for western medicine, we can observe changes of fasting glucose and glycosylated hemoglobin (HbA1c) values of diabetic patients. After measuring fasting glucose and glycosylated hemoglobin values of diabetic patients, the diabetic patients dose with one or two MetaJust tablets after meals with 3~6 tablets a day continuously for 3~6 months, then measuring fasting glucose and glycosylated hemoglobin values again after 3~6 months.

Fasting glucose levels between MetaJust before and after treatment to

diabetic patients for one to three months are compared. With reference to FIG. 9 for the clinical results of fasting glucose levels between MetaJust before and after treatment to diabetic patients for one to three months, the results show that there is significant improvement for the blood glucose value from original average 192 mg/dl to 133 mg/dl with high pitch difference of 59 mg/dl. With reference to FIG. 10 for the clinical results of glycosylated hemoglobin (HbA1c) levels between MetaJust before and after treatment to diabetic patients for three to six months, the results show that there is a significant effect of the lower glycosylated hemoglobin (HbA1c) value from original average 8.08 % to 7.51 % with difference of 0.57 %, indicating that MetaJust can definitely improve the blood glucose value of the diabetes and metabolic syndrome.

WHAT IS CLAIMED IS:

1. A multi-herbal medicinal composite for treating the metabolic syndrome, and said multi-herbal medicinal composite comprising:
Bidens pilosa, occupying 65%~95% of the composite by weight; and
Panax ginseng, occupying 5%~35% of the composite by weight.
2. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite comprises 80 wt% *Bidens pilosa* and 20 wt% *Panax ginseng*.
3. The multi-herbal medicinal composite as recited in claim 1, wherein said *Bidens pilosa* is in the form of leaf and stem portion of dried *Bidens pilosa*.
4. The multi-herbal medicinal composite as recited in claim 1, the used species of *Bidens pilosa* is *B. pilosa* var. *radiata*.
5. The multi-herbal medicinal composite as recited in claim 1, wherein said *Panax ginseng* is red ginseng.
6. The multi-herbal medicinal composite as recited in claim 1, wherein said *Bidens pilosa* and said *Panax ginseng* are in the form of extract.
7. The multi-herbal medicinal composite as recited in claim 6, wherein the extract form of said *Bidens pilosa* and said *Panax ginseng* is in the form of aqueous extract.
8. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite is made in the form of a tablet, grain, powder, liquid, capsule or honeyed pill.

9. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite is able to add into drinks, meals or other food products.
10. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite has a function of regulating blood glucose.
11. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite has a function of promoting insulin secretion.
12. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite has a function of reducing insulin resistance.
13. The multi-herbal medicinal composite as recited in claim 1, wherein said multi-herbal medicinal composite is provided for curing diabetes.
14. A preparation method of a multi-herbal medicinal composite for treating a metabolic syndrome, and the method comprising the steps of:
 - (a) mixing *Bidens pilosa* and *Panax ginseng* to form a main raw material according to the respective weight percentage given by claim 1;
 - (b) extracting the main raw material by an appropriate solvent to obtain an extract liquid;
 - (c) filtering the extract liquid, and then concentrating the filtered extract liquid; and
 - (d) drying the concentrated extract liquid.
15. The preparation method of the multi-herbal medicinal composite as recited

in claim 14, wherein said extraction process includes the first extraction process, the second extraction process and the third extraction process.

16. The preparation method of the multi-herbal medicinal composite as recited in claim 15, wherein said the first extraction process is the main raw material heated up with an appropriate solvent having a volume equal to 20~40 times of main raw material at 80~100 °C for 30~50 minutes.
17. The preparation method of the multi-herbal medicinal composite as recited in claim 15, wherein said the second extraction process is the main raw material heated up with an appropriate solvent having a volume equal to 20~40 times of main material at 80~100 °C for 40~70 minutes.
18. The preparation method of the multi-herbal medicinal composite as recited in claim 15, wherein said the third extraction process is the main raw material heated up with an appropriate solvent having a volume equal to 20~40 times of main material at 80~100 °C for 40~70 minutes.
19. The preparation method of the multi-herbal medicinal composite as recited in claims 16 to 18, wherein said appropriate solvent is water heated to 80~100 °C.
20. The preparation method of the multi-herbal medicinal composite as recited in claims 14 to 18, wherein said appropriate solvent is water.
21. The preparation method of the multi-herbal medicinal composite as recited in claim 15, wherein said drying step adopts a spray method or a freeze drying method.