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(54) Title: METHOD AND COMPOSITION FOR PREVENTING OR REDUCING THE SYMPTOMS OF INSULIN RESISTANCE SYNDROME

(57) Abstract: A method for preventing and/or reducing the symptoms of insulin resistance and a related syndrome in persons comprises identifying persons having or at risk for having such symptoms, and administering to them an effective amount of a composition comprising niacin-bound chromium that prevents or reduces the symptoms. Compositions incorporating niacin-bound chromium and additional compounds also are disclosed that are particularly effective in synergistically preventing or reducing these symptoms.

## METHOD AND COMPOSITION FOR PREVENTING OR REDUCING THE SYMPTOMS OF INSULIN RESISTANCE SYNDROME

### BACKGROUND OF THE INVENTION

The present invention relates generally to a method and composition for preventing or reducing the symptoms of insulin resistance syndrome in a person.

An insulin resistance syndrome that has been identified as "Syndrome X" by previous research is a common metabolic disorder affecting more than 75 million Americans to some degree. Insulin resistance is a condition in which the body becomes resistant to its own insulin. The body of the person affected compensates by releasing more insulin, elevating body insulin levels. This elevated insulin level leads to increased risk of a variety of symptoms, including diabetes, obesity, and heart disease.

Syndrome X appears to be highly prevalent in the obese. Individual elements of Syndrome X (obesity, hypertension, lipid disturbances, and glucose intolerance) are frequently encountered during a typical person's life span, and they tend to be increasing apparent as people age, usually becoming most prevalent after age 35. Theoretical considerations suggest that insulin resistance may be a primary factor that plays a causative role in the induction of both obesity and diabetes. Atherogenic risk factors associated with obesity and Syndrome X contribute independently to the development of atherosclerotic disease, and risk of a cardiovascular event increases sharply with the burden of risk factors associated with obesity.

Animal models of Syndrome X, as observed in rats fed high fat diets, exhibit excess accumulation of muscle triglyceride coincident with development of insulin resistance. This also seems to occur in humans; several studies demonstrate increased muscle triglyceride content in insulin resistant states. There is substantial evidence indicating that excess muscle and liver lipid accumulation causes or exacerbates insulin resistance in Syndrome X and in Type II diabetes. Development of strategies to prevent this, therefore, seem worthwhile.

Avoiding weight gain from adolescence to middle age is known to reduce cardiovascular morbidity and mortality. Despite much debate in the past regarding the influence of obesity on health and the benefits of maintaining normal weight, it is clear that changes in weight correlate to changes in several atherogenic risk factors. Recent perspective studies indicate a continuous graded influence of body mass index (BMI), the ratio of weight expressed in kilograms divide by the height meters squared, on the rate of coronary disease development. Increased risk is evident at BMI levels below average, indicating that moderate obesity can be unhealthy. Central obesity, typically including measurements of waist girth or waist to hip ratio, has been shown to be more metabolically disadvantageous than other forms of obesity and, as a consequence, it is considered a strong predictor of cardiovascular disease.

The mechanism whereby obesity and weight gain promote atherogenic risk factors and, in turn, cardiovascular disease is well established. Excess body fat has been shown to increase resistance to insulin action and reduce uptake of glucose by peripheral tissues. Abdominal obesity, in particular, is associated with insulin resistance, hyperinsulinemia, a relative deficiency of lipoprotein lipase, elevated triglycerides, reduced HDL-cholesterol and small dense LDL-particles. Obesity may promote increased absorption in the renal tubules, expanding blood volume and inducing an autonomic imbalance that results in hypertension. In addition, insulin

resistance often eventuates into glucose intolerance and diabetes which in turn accelerates atherogenesis.

Obesity is clearly the most prevalent metabolic disorder in the United States, and weight control deserves a high priority to curb cardiovascular disease and the associated predisposing conditions, such as lipidemia, hypertension and glucose intolerance. The benefits of weight control on the major atherogenic risk factors and the insulin resistance syndrome should provide a strong incentive and rationale for control of obesity. There is no other risk factor that affects the cardiovascular risk profile as strongly. It is well known that non-insulin dependent type II diabetes is highly associated with obesity. It has been reported that healthy persons with elevated insulin levels have increased levels of LDL cholesterol, decreased HDL cholesterol and high blood pressure compared with healthy individuals who have normal insulin levels. Diabetes is associated with high blood lipids, hypertension and a tendency of blood platelets to clot, which can block arteries resulting in heart attack or stroke. Diabetes causes a defect in glucose homeostasis. Weight control is a logical first approach to avoid moderate degrees of hypertension, dyslipidemia, glucose tolerance and hyperinsulinemia that constitute Syndrome X.

To overcome glucose tolerance, patients with syndrome X secrete large amounts of insulin. Treatment of Syndrome X should therefore be aimed at:

- 1) increasing insulin sensitivity; 2) attenuating day-long hyperinsulinemia; and
- 3) pharmacologic treatment of the specific manifestations of syndrome X, if lifestyle interventions such as weight loss are not entirely successful. The two major lifestyle modulators of insulin action are body weight and physical fitness; the heavier and the more sedentary a patient is, the greater the degree of insulin resistance and compensatory hyperinsulinemia.

However, even with control of weight, many people can still develop Syndrome X. Also, many people find controlling their weight to be difficult, and they are unsuccessful in their attempts. Therefore, pharmacological treatments are needed to help reduce the effects of Syndrome X in persons.

Chromium helps insulin metabolize fat, turn protein into muscle and convert sugar into energy. It is an essential trace element required for normal protein, fat and carbohydrate metabolism. Chromium levels are known to decrease with age, and marginal chromium deficiencies appear to be widespread. Chromium is important for energy production and plays a role in regulating appetite, reducing sugar cravings, and increasing lean body mass.

Niacin-bound chromium (also called chromium nicotinate or chromium polynicotinate) dramatically increases the effectiveness of chromium in a person ingesting it. Normally, chromium is poorly absorbed and utilized by the body. However, researchers have found that the most potent form of chromium in nature is that form bound to the B-vitamin, niacin. Furthermore, previous research discoveries led to the identification of Glucose Tolerance Factor or "GTF", a biologically active form of chromium that facilitates normal insulin function, which is responsible for normal glucose (blood sugar) metabolism. Researchers have found that a particular oxygen-coordinated chromium niacin complex is the most potent form of all, being over eighteen times more potent than the next closest form of niacin-bound chromium tested.

In 1997, researchers at the University of Texas, Austin, showed that a combination of administration of niacin-bound chromium along with exercise in obese women resulted in a significant weight loss in the women and also lowered the increase in insulin levels when the women were orally fed glucose. In contrast, those

taking chromium picolinate, a different form of chromium, were found to show significant weight gain. In 1999, researchers at Georgetown University Medical Center showed that compared to a placebo, niacin-bound chromium caused significant loss of body fat and sparing of muscle (lean body mass) in overweight African-American women. Also, tests on the blood chemistries of the women revealed no significant adverse effects from the ingestion of 600  $\mu$ g of elemental chromium daily for 2 months. This observation demonstrated the safety of administration of niacin-bound chromium at the tested levels.

In 1994, researchers at Auburn University showed that supplementation with 200 mcgs of niacin-bound chromium significantly lowered moderate levels of cholesterol by an average of 14 percent and improved the ratio of total cholesterol to HDL ("good") cholesterol by 7 percent in male athletes. In 1995, researchers at Georgetown University Medical Center showed that a combination of niacin-bound chromium and soluble fiber (*i.e.*, guar) significantly inhibited sugar-induced high blood pressure in rats. In 1997, researchers at Georgetown University Medical Center showed that niacin-bound chromium inhibited sugar-induced high blood pressure, improved long-term blood sugar status and reduced liver and kidney lipid peroxidation in rats. In 2000, researchers at Georgetown University Medical Center showed that a combination of niacin-bound chromium and grape seed proanthocyanidin extract significantly lowered both total cholesterol levels and LDL ("bad") cholesterol levels by 10 and 14 percent, respectively, in people with elevated blood cholesterol levels.

Diabetic patients have been found to have lower serum chromium levels and a higher chromium excretion rate. Treatment with niacin-bound chromium has been found to improve glucose tolerance in diabetic patients. Dietary trivalent chromium has been shown to have significant beneficial effects on the insulin system.

It has been demonstrated that essential hypertension may be due to insulin perturbations. As high dose chromium supplementation seems nontoxic, chromium may prove to be a useful means to lower blood pressure in some essential hypertensives as well as diabetic hypertensives. It also has been shown that chromium supplementation may prove to be the most useful means to prevent or treat type II diabetes mellitus and related cardiovascular disorders. Chromium supplementation amplifies insulin receptor tyrosine kinase activity, which explains the relationship between chromium and its effects in diabetes. Chromium further reduces vascular smooth muscle calcium loads and thus reduces peripheral vascular resistance in insulin-resistant states.

Recently, the U.S. Department of Agriculture (USDA) found that many middle-age diabetics could overcome their symptoms by taking a chromium supplement. The USDA's findings suggest that very low chromium intakes may be putting millions of Americans on the road to diabetes (and high blood cholesterol) and that the process could be reversed by supplementing with chromium. A separate study found that marginal chromium loss in male athletes resulting in impaired insulin function can be improved by supplementation with niacin-bound chromium.

However, though the above studies demonstrate that administering niacin-bound chromium may serve as a beneficial therapeutic method for reducing or preventing the various symptoms associated with Syndrome X, this has not been entirely effective. Improved methods and compositions, therefore, are necessary to provide for preventing or and reducing the symptoms of Syndrome X in persons. The present invention fulfills this need and provides for further advantages.

#### SUMMARY OF THE INVENTION



The present invention resides in a method for preventing or reducing the symptoms of insulin resistance in a person, the method comprising: identifying a person suffering from or at risk for suffering from the symptoms; and administering a composition comprising (-) hydroxycitric acid and an effective amount of niacin-bound chromium that, when administered to the person, alleviates the symptoms, wherein the composition further comprises two compounds selected from the group consisting of zinc, trans-resveratrol, gymnemic acid, selenium, an anthocyanidin, allicin, and a saponin, and wherein the amount of (-) hydroxycitric acid in the composition is between about 250 and about 2,500 mg.

In a preferred form, the method incorporates administering a composition comprising between about 50 and about 1,000 µg niacin-bound chromium, and the composition is administered in two doses per day.

Preferably, if present, the amount of the amount of zinc in the composition is between about 5 and about 50 mg, the amount of trans-resveratrol in the composition is between about 5 and about 50 mg, the amount of gymnemic acid in the composition is between about 50 and about 200 mg, the amount of selenium in the composition is between about 0.025 mg and about 0.1 mg, the amount of anthocyanidin in the composition is between about 5 and about 50 mg, the amount of allicin in the composition is between about 2 and about 8 mg, and the amount of saponin in the composition is between about 100 and about 300 mg.

The present invention also resides in a composition comprising niacin-bound chromium, (-) hydroxycitric acid and two compounds selected from the group consisting of zinc, trans-resveratrol, gymnemic acid, selenium, an anthocyanidin, allicin, and a saponin, and wherein the (-) hydroxycitric acid composition comprises between about 250 and about 2,500 mg.

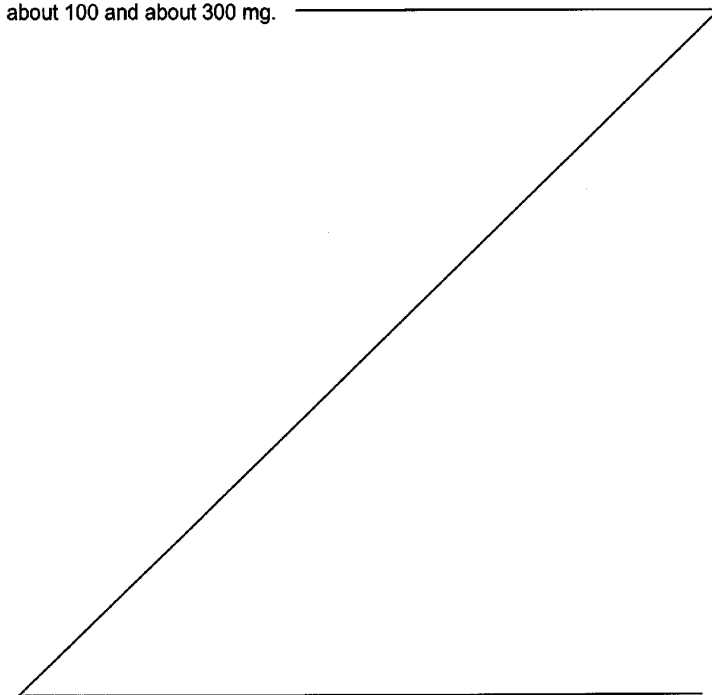
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In a preferred form the composition comprises between about 50 and about 1,000 µg niacin-bound chromium.

- 5 Preferred compositions include those where the amount of zinc in the composition is between about 5 and about 50 mg, the amount of trans-resveratrol in the composition is between about 5 and about 50 mg, the amount of gymnemic acid in the composition is between about 50 and about 200 mg, the amount of selenium in the composition is between about 0.025 mg and about 0.1 mg, the amount of anthocyanidin in the composition is between about 5 and about 50 mg, the amount of allicin in the composition is between about 2 and about 8 mg, and the amount of saponin in the composition is between about 100 and about 300 mg.
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## DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

The present invention resides in a method for preventing or reducing the symptoms of Syndrome X in a person, incorporating a step of identifying a person having the Syndrome, and then administering an amount of niacin-bound chromium to the person sufficient to prevent or reduce the symptoms of the Syndrome. The present invention also resides in compositions incorporating niacin-bound chromium that, when ingested in sufficient quantity by a person, prevent or reduce the symptoms of Syndrome X in the person.

The method of the present invention involves first identifying a person having Syndrome X. A diagnosis of Syndrome X is made based on observing some or all of the following common symptoms: impaired glucose tolerance, hyperinsulinemia, diabetes, hypertriglyceridemia, elevated LD cholesterol, low HDL cholesterol, hypertension, diabetes, and hypertension. Then, the person is administered an effective amount of niacin-bound chromium, on a daily basis. Preferably, the amount of niacin-bound chromium administered to an adult ranges from about 100 to about 1000 micrograms per day, taken in two daily doses. The niacin-bound chromium preferably is administered orally in a variety of forms, including capsule, tablet, beverage, food additive, powder, liquid, or food.

Preferred aspects of the method of the present invention involve administration of additional compounds along with the niacin-bound chromium, including: one or more of the following: (-)hydroxycitric acid; zinc, preferably from zinc methionine; *trans*-resveratrol; gymnemic acid; selenium; anthocyanidins, preferably from bilberry, blueberry, or grape seed extracts; allicin, preferably from garlic; and saponins, preferably from fenugreek. These components work synergistically with the niacin-bound chromium to improve its function in alleviating

the symptoms of Syndrome X. Particularly preferred compositions administered include any three of the components in the following amounts: 50 to 1000 µg niacin-bound chromium; 250 to 2500 mg (-)hydroxycitric acid; 5 to 50 mg zinc; 1 to 5 mg *trans*-resveratrol; 50 to 200 mg gymnemic acid; 0.025 to 0.1 mg selenium; 5 to 50 mg anthocyanidins; 2 to 8 mg allicin; and 100 to 300 mg saponins.

#### EXAMPLE

Studies were conducted to evaluate the efficacy of a combination of natural products, including niacin-bound chromium, on lowering high blood pressure, one of the particular symptoms commonly associated with Syndrome X. One half of a group of 100 normotensive rats were fed a diet containing the following: chromium nicotinate at a human equivalency dosage of 400 µg of elemental chromium (marketed under the brand name ChromeMate by InterHealth Nutraceuticals of Benicia, California), zinc methionine (marketed under the brand name OptiZinc by InterHealth Nutraceuticals), and grape seed extract incorporating proanthocyanidins (marketed under the brand name ActiVin by InterHealth Nutraceuticals). The rats that were placed on diets containing supplemental chromium nicotinate had significantly lowered blood pressure and lipid peroxidation in their livers and kidneys than rats fed normal diets. Sugar-induced hypertension also was reduced in the rats, along with hepatic and renal lipid peroxidation and glycosylated hemoglobin levels.

Although the invention has been disclosed in detail with reference only to the preferred embodiments, those skilled in the art will appreciate that additional methods and compositions can be made without departing from the scope of the invention.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:

1. A method for preventing or reducing the symptoms of insulin resistance in a person, the method comprising:  
identifying a person suffering from or at risk for suffering from the symptoms; and  
administering a composition comprising (-) hydroxycitric acid and an effective amount of niacin- bound chromium that, when administered to the person, alleviates the symptoms, wherein the composition further comprises two compounds selected from the group consisting of zinc, trans-resveratrol, gymnemic acid, selenium, an anthocyanidin, allicin, and a saponin, and  
wherein the amount of (-) hydroxycitric acid in the composition is between about 250 and about 2, 500 mg.
2. A method as defined in claim 1, wherein the step of administering an amount of the composition incorporates administering a composition comprising between about 50 and about 1,000 µg niacin-bound chromium.
3. A method as defined in claim 1, wherein the step of administering comprises administering the composition in two doses per day.
4. A method as defined in claim 1, wherein the amount of zinc in the composition is between about 5 and about 50 mg.
5. A method as defined in claim 1, wherein the amount of trans- resveratrol in the composition is between about 5 and about 50 mg.
6. A method as defined in claim 1, wherein the amount of gymnemic acid in the composition is between about 50 and about 200 mg.

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7. A method as defined in claim 1, wherein the amount of selenium in the composition is between about 0.025 mg and about 0.1 mg.
8. A method as defined in claim 1, wherein the amount of anthocyanidins in the composition is between about 5 and about 50 mg.
9. A method as defined in claim 1, wherein the amount of allicin in the composition is between about 2 and about 8 mg.
10. A method as defined in claim 1, wherein the amount of saponins in the composition is between about 100 and about 300 mg.
11. A composition comprising niacin-bound chromium, (-) hydroxycitric acid and two compounds selected from the group consisting of zinc, trans-resveratrol, gymnemic acid, selenium, an anthocyanidin, allicin, and a saponin, and wherein the (-) hydroxycitric acid composition comprises between about 250 and about 2,500 mg.
12. A composition as defined in claim 11, wherein the composition comprises between about 50 and about 1,000 µg niacin-bound chromium.
13. A composition as defined in claim 11, wherein the composition comprises between about 5 and about 50 mg zinc.
14. A composition as defined in claim 11, wherein the composition comprises between about 5 and about 50 mg trans-resveratrol.
15. A composition as defined in claim 11, wherein the composition comprises between about 50 and about 200 mg gymnemic acid.
16. A composition as defined in claim 11, wherein the composition comprises between about 0.025 and about 0.1 mg selenium.

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17. A composition as defined in claim 11, wherein the composition comprises between about 5 and about 50 mg anthocyanidins.
18. A composition as defined in claim 11, wherein the composition comprises between about 2 and about 8 mg allicin.
19. A composition as defined in claim 11, wherein the composition comprises between about 100 and about 300 mg saponins in the composition is between about 100 and about 300 mg.
20. A method for preventing or reducing the symptoms of insulin resistance in a person substantially as hereinbefore described with reference to the example.
21. A composition substantially as hereinbefore described with reference to the example.

Dated this 2<sup>nd</sup> day of November 2006

**Interhealth Nutraceuticals, Inc.**

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