“An ideal regimen to fight against the single most important metabolic disease which can affect nearly every organ system in the body”

Super Natural Sugar Balance

Insululike™
A Nutriphenotypic Approach

* Inhibition of Glucose absorption
* Stimulates insulin secretion/action
* Prevents PUFA peroxidation
* Improves capillary function
* Improves insulin binding
* Improves insulin sensitivity

Helps to support the benefits of controlling diabetes beyond the Glucose Metabolism & Cardiovascular function

CONTENTS
1. Introduction
2. Metabolic Syndrome - An Overview
3. Causes of Metabolic Syndrome
4. Traditional approach for Type-II Diabetes Insulin Therapy
5. Insululike - A Nutri Phenotypic Approach Ingredients
   * Eugenia Jambolana Extract
   * Curcuminoids
   * Berberine Hydrochloride
   * Cynanins
   * Banaba Leaf Extract
   * Charantin
   * Methylhydroxy chalcone polymers
   * 4-Hydroxy isoleucine
   * Anthocyanins
   * Alphalipoic acid
   * Chromium
   * Vitamin C, D3, E, K & Biotin
   * Benfotiamine
   * Amino acids - Isoleucine, Glycine, N-Acetyl cysteine, L-Glutathione
6. Insululike - A Nutri Phenotypic Approach specific nutrients in Insululike with the biochemical and genetic effects to help protect from disease
7. Lactonova awareness information -Life support benefits of exercise & stress management
8. Benefits of slow release
9. Conclusion - Future direction
10. Prescribing info & References

A Product Review
Although metabolic syndrome (commonly referred to as MetS) is a somewhat elusive diagnosis, the health ramifications can be of significant consequence. There is no agreed upon definition of MetS, but the current consensus between the International Diabetes Foundation and the American Heart Association/National Heart, Lung, and Blood Institute is that MetS is defined as the presence of three or more of the following:

- Increased waist circumference ($\geq 102$ centimeters/40 inches in men and $\geq 88$ centimeters/34 inches in women)
- Elevated blood pressure ($\geq 130/85$ mmHg)
- Elevated blood sugar (fasting glucose $\geq 100$ mg/dL)
- High triglycerides ($\geq 150$ mg/dL)
- Low high-density lipoprotein (HDL) cholesterol (<40 mg/dL in men and <50 mg/dL in women)

Non-alcoholic Fatty Liver Disease (NAFLD)

NAFLD is closely associated with metabolic syndrome (its incidence increases as weight increases). NAFLD is the primary cause of elevated liver enzymes. Liver enzymes should be tested in all patients with suspected MetS, and MetS with a fatty liver comorbidity should be ruled out in patients with elevated liver enzymes. Weight loss and addressing other aspects of MetS are central to treatment of fatty liver.

Cardiovascular Disease / Diabetes

Individuals with MetS are three times more likely than those without MetS to have a stroke or a heart attack, and twice as likely to die from these events. The risk of developing type II diabetes is five times higher in patients with MetS.

INTRODUCTION

Diabetes mellitus is chronic metabolic disorder that has a significant impact on the health, quality of life and life expectancy of patients, as well as on the health care system. In India it is estimated that presently 19.4 million individuals are affected by this deadly disease, which is likely to go up by 57.2 million by the year 2025. Diabetes is divided into two major categories: Type 1 diabetes (formerly known as insulin dependent diabetes mellitus or IDDM) and Type 2 diabetes (formerly known as non-insulin dependent diabetes mellitus or NIDDM) the overall prevalence of diabetes is approximately 60% of the population of which 90% is Type 2. Type 2 diabetes represents a syndrome with disordered metabolism of carbohydrate and fat. The most prominent clinical feature is hyperglycemia (fasting plasma glucose level >126mg/dL, or glycated hemoglobin Alc (Hb Alc) > 6.9%). In most patients with Type 2 diabetes the onset is in adulthood most commonly in obese people over 40 years of age. Hypertension, hyperlipidemia and atherosclerosis are often associated with diabetes.

Table 1. Association between BMI and MetS Risk for Men and Women

<table>
<thead>
<tr>
<th>BMI / Gender</th>
<th>Prevalence of MetS</th>
<th>Risk Compared to Normal Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &lt;25 (normal or underweight males)</td>
<td>7%</td>
<td>Base line</td>
</tr>
<tr>
<td>BMI 25-29.9 (Overweight males)</td>
<td>30%</td>
<td>6 times the risk</td>
</tr>
<tr>
<td>BMI = 30 (obese males)</td>
<td>65%</td>
<td>32 times the risk</td>
</tr>
<tr>
<td>BMI = 25 (normal or underweight females)</td>
<td>9%</td>
<td>Base line</td>
</tr>
<tr>
<td>BMI 25-29.9 (overweight females)</td>
<td>33%</td>
<td>5.5 times the risk</td>
</tr>
<tr>
<td>BMI = 30 (obese females)</td>
<td>56%</td>
<td>17 times the risk</td>
</tr>
</tbody>
</table>

MetS is associated with increased risks for a number of comorbidities, including cardiovascular disease, Type 2 diabetes, fatty liver, polycystic ovary syndrome (PCOS), and sleep apnea.


Non-alcoholic Fatty Liver Disease (NAFLD)

NAFLD is closely associated with metabolic syndrome (its incidence increases as weight increases). NAFLD is the primary cause of elevated liver enzymes. Liver enzymes should be tested in all patients with suspected MetS, and MetS with a fatty liver comorbidity should be ruled out in patients with elevated liver enzymes. Weight loss and addressing other aspects of MetS are central to treatment of fatty liver.
Sleep Apnea
Obesity is at the heart of the worldwide increase in the prevalence of sleep apnea, a condition commonly associated with MetS. In addition to the epidemiological association between the two, it appears that imbalances brought on by sleep apnea contribute to some of the symptoms seen in MetS. For instance, studies indicate sleep apnea increases cortisol levels, which are in turn associated with obesity and insulin resistance. As many as 70 percent of obese Type 2 diabetics experience sleep apnea.

Polycystic Ovary Syndrome (PCOS)
Many aspects of metabolic syndrome are also observed in women who have PCOS — including insulin resistance, obesity in some cases, and dyslipidemia. Statistics indicate approximately 30 percent of women with PCOS have impaired glucose tolerance, while an additional 7.5 percent have diabetes. All women with a diagnosis of PCOS or symptoms suggesting a diagnosis of PCOS (infertility, hirsutism, and oligomenorrhea) should be tested for hyperglycemia and dyslipidemia.

How to Determine Body Mass Index
Multiply weight in pounds by 703 Square the height in inches Divide the first number (weight x 703) by the second number (height squared)

Alternate metric method:
Divide weight in kilograms by height in meters squared (kg/m2)

The Inflammation Connection
Obesity is known to be associated with low-level inflammation. The inflammation occurs first in the adipocytes, with an increase in tumor necrosis factor-alpha (TNF-α). TNF-α stimulates a more general inflammatory state that can ultimately result in insulin resistance and endothelial dysfunction, which can contribute to hypertension and other vascular complications (Figure 1).

What Causes Metabolic Syndrome?
Proposed unbalanced mechanisms

1. Nutrient Deficiencies
Although it is easy to consider metabolic syndrome as attributable to excesses, there are several nutrient deficiencies associated with this condition. The most extensively researched deficiencies are magnesium, vitamin D, and chromium.

MAGNESIUM
Magnesium is one of the most clearly identified nutrient deficiencies in patients with MetS. Prior to identifying it as “metabolic syndrome,” researchers were examining the combination of insulin resistance, hyperinsulinemia, essential hypertension, ischemic heart disease, and magnesium deficiency (Reaven-Modan syndrome). Studies clearly show that insulin sensitivity declines in healthy subjects when a state of magnesium deficiency is induced. A large, prospective, 15-year study of young American adults found a 31-percent increase in MetS in the group of subjects with the lowest magnesium intake. A study on hair mineral content found lower magnesium-to-calcium ratios in individuals with insulin resistance. Lower intakes and lower blood levels of magnesium are associated with an elevation in inflammatory markers, while higher magnesium intakes and higher blood levels demonstrate a protective effect. As discussed above, these inflammatory markers are associated with MetS.

VITAMIN D
Vitamin D plays a role in MetS. Studies show vitamin D has a role in immune system function, inflammation, parathyroid levels, pancreatic beta-cell function, and mineral balances that are key to the pathogenesis of the disorder. A meta-analysis of 28 studies showed that, when compared to higher vitamin D levels, lower serum levels of 25-hydroxyvitamin D were associated with a 55-percent increase in diabetes, a 33-percent increase in the risk of cardiovascular diseases, and a 51-percent increase in metabolic syndrome.

CHROMIUM
Chromium is not found in sufficient amounts in food to replenish tissue stores or to affect clinically significant improvement in blood glucose control. Current estimates indicate 80 percent of Americans are deficient in this essential mineral nutrient, and diets high in simple sugars can deplete chromium from the body. In a study of 123 males (63 with MetS; 60 controls), those with MetS had lower hair chromium concentrations than healthy controls.
2. Dietary Excesses

**SUGAR-SWEETENED SODAS**
When examining the effects of sugar-sweetened beverages on MetS parameters, researchers found plasma triglycerides and waist circumference, both aspects of MetS, increased as the number of sugared beverages increased\(^\text{16}\).

**DIET SODAS**
As awareness of the negative effects of sugar-sweetened sodas has increased, many people who choose diet sodas have the misconception that these beverages provide a healthier choice. Unfortunately, data indicates the opposite to be true. Individuals with an “at least daily” intake of diet soda were shown to have a 36-percent greater risk of developing metabolic syndrome and a 67-percent greater risk of developing type 2 diabetes compared to individuals who consumed no diet beverages\(^\text{17}\).

**HIGH-FRUCTOSE CORN SYRUP (HFCS)**
Studies comparing HFCS-sweetened beverages to sugar-sweetened beverages show HFCS-containing beverages increase MetS symptoms at a higher rate than other sugar-containing beverages\(^\text{18,19}\). Other research has outlined the potential health outcomes associated with HFCS (Table 2)\(^\text{20}\).

Forty-eight percent of Indians drink an average of one soda daily, putting them at greater risk for MetS or type 2 diabetes.

3. Other Dietary Excesses
In evaluating questionnaires from different subjects that compared dietary factors and MetS incidence for nine years, researchers found “consumption of a Western dietary pattern” that is high in meat, fried foods, and diet soda promoted the development of metabolic syndrome\(^\text{21}\).

**Lack of Exercise**
Lack of physical activity has long been associated with adverse impacts on metabolic health, including an increase in abdominal fat and a decrease in insulin sensitivity. As a person becomes less active, BMI, waist-hip ratio, waist circumference, and obesity go up\(^\text{22}\). Even in adolescents, lack of exercise and low cardio-respiratory fitness are associated with increased risk for MetS\(^\text{23}\).

**Environmental Toxin Exposure**
Increasing evidence over the past decade indicates that chemicals in the environment can contribute to the hormonal imbalances that result in metabolic disruption in society at large. Human epidemiological data and numerous animal studies specifically associate endocrine-disrupting chemicals, such as organochlorine pesticides (like DDT), dioxins (like PCBs), and flame retardants (PBDEs), with metabolic syndrome. Studies also link exposure to the plasticizing agents bisphenol-A (BPA) and phthalates to insulin resistance, obesity, and liver abnormalities.

Researchers are concerned that the effects of these chemicals will be amplified because chemical production now exceeds 400 million tons globally\(^\text{24}\). BPA has been shown to have significant adverse effects on estrogen signaling, even at small doses\(^\text{25}\). This signaling can alter glucose transporter function, cause hyperglycemia, interfere with hypothalamic regulation of weight, result in adiposity, and impair energy expenditure\(^\text{26}\).

Most chronic health problems, including stubborn weight gain, unrelenting fatigue, high blood pressure, creeping cholesterol, and high blood sugar, are not found in simply one organ, but in several parts of the body. This is the result of years of slow, subtle challenges to one's unique metabolism.

Lifestyle habits, stress levels, prescription drug use, relationships, inherited genes, and the environment can all dictate one's current state of health. Cracking the Metabolic Code helps both practitioner and patient understand how these factors can affect health and what can be done to reverse them.
4. Stress
Stress is a well-known contributing factor to obesity. In a study of 10,308 men and women ages 35-55, workplace stress measured over a 14-year period was positively associated with an increased risk for metabolic syndrome. Employees with chronic work stress were twice as likely to develop MetS than individuals without work stress.

**How can stress cause metabolic syndrome?**
Figure 2 illustrates some of the factors involved. For a more detailed discussion on the relationship between hormones, neurotransmitters, and metabolism, the book Cracking the Metabolic Code is highly recommended.

**Laboratory Evaluation**
The basic markers for diagnosis and follow-up of MetS patients include the measuring of waist circumference, blood pressure, blood sugar, triglycerides, and cholesterol fractions (see page 1 for abnormal levels of these diagnostic markers for MetS). The goal is to achieve the following:

- women: waist circumference <34 inches; men: waist circumference <40 inches
- blood pressure ≤120/80 mmHg
- fasting blood sugar <100 mg/dL
- triglycerides <150 mg/dL
- HDL-cholesterol levels >50 mg/dL in women and >40 mg/dL in men

In cases of suspected MetS, serum liver enzymes should be tested. Laboratories offer additional markers to determine the state of long-term blood sugar levels (HbA1c), inflammation (e.g., high sensitivity C-reactive protein, TNF-α), insulin secretion (e.g., insulin, proinsulin, and C-peptide), thrombosis (e.g., plasminogen activator-I [PAI-1] and fibrinogen), and fat metabolism associated hormones (e.g., adiponectin and leptin). Hormones produced in fat cells – adiponectin and leptin are shown to have an increasing role in regulating inflammation, insulin sensitivity, appetite, and energy metabolism.

**TRADITIONAL APPROACH FOR TYPE-II DIABETES INSULIN THERAPY**
Insulin is usually added to an oral agent when glycemic control is suboptimal at maximal doses of oral medications. (Table 1 summarizes various limitations of current drug therapies.)

**Table 1. Limitations of Hypoglycemic Medications**

<table>
<thead>
<tr>
<th>Anti-diabetic Drugs</th>
<th>Mechanism of action</th>
<th>Limitations/Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sulfonylureas</td>
<td>Enhance insulin secretion from the pancreatic beta cells</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>Biguanides</td>
<td>Reduce plasma glucose via inhibition of hepatic glucose production &amp; increase muscle glucose uptake</td>
<td>Gastrointestinal disturbances</td>
</tr>
<tr>
<td>Alpha-glucosidase inhibitors</td>
<td>Decrease postprandial plasma glucose by slowing carbohydrate partition &amp; designing gastric absorption</td>
<td>Gastrointestinal disturbances</td>
</tr>
<tr>
<td>Thiazolidinediones</td>
<td>Improving insulin sensitivity in the muscles to a much lesser extent in the liver</td>
<td>Liver toxicity, weight gain, high LDL cholesterol, high cost</td>
</tr>
<tr>
<td>Meglitinides</td>
<td>Augment insulin secretion</td>
<td>Hypoglycemia, weight gain</td>
</tr>
<tr>
<td>Insulin</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

**PHARMACOLOGICAL TREATMENT & LIMITATIONS**
By conventional standards, oral therapy is indicated in any patient with Type 2 diabetes in whom diet & exercise fail to achieve acceptable glycemic control. Although initial responses may be good oral hypoglycemic drugs may lose their effectiveness in a significant percentage of patients. The drug categories include sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinides.

INSULIKE contains all essential natural botanicals and nutrients to address factors associated with MetS* and specifically diabetes.

INSULIKE contains vitamins and minerals often found to be deficient in MetS, diabetic patients, for example, each serving contains 400 IU (10mcg) of vitamin D3, 40 mg of vitamin C and 40 mcg chromium* and 55mcg of selenium.

EUGENIA JAMBOLANA EXTRACT

Eugenia Jambolana is a fruit; it is a flavonoid rich extract. It is long known for its Anti diabetic activity in traditional medicines. Studies have proved that the various biological parameters such as glucose tolerance, lipid profile, glycogen biosynthesis, glucose uptake and insulin release. It has a dual hypoglycemic and hypolipidemic effect.

INSULIKE contains the seed extract of Eugenia Jambolana Extract this botanical was heavily researched in Europe as an anti-diabetic agent prior to insulin development. Unpublished research on the specific extract Eugenia Jambolana Extract found a 20-percent decrease in blood sugar levels after a carbohydrate load (50 grams of white rice) in healthy volunteers (Figure 4). Another unpublished study conducted on 40 patients with Type 2 diabetes found Eugenia Jambolana Extract (average 2-3 grams daily) resulted in a 35-percent reduction in fasting blood sugar after 15 days and a 49-percent reduction after 90 days Figure 4.

Bhavna Sharma, G. Viswanath, Rajani Salunke, parta Roy
In a small, unpublished pilot study, 13 Type 2 diabetics (nine were not on oral hypoglycemic medications) were given varying dosages of Eugenia Jambolana Extract (from 1.5-6 g daily) for 10 weeks. Fasting blood sugar dropped an average of 33 percent (n=12), while postprandial blood sugar dropped an average of 35 percent (n=10) (Figure 6).*

Eugenia Jambolana Extract was evaluated at a hospital at doses of 1-6 g (average 1.5 to 3 g) for periods from two weeks to six months. Significant decreases in fasting blood sugar were reported in several evaluations of Type 2 diabetics (ranging from 13 to 112 subjects).* In two smaller observational studies, Eugenia Jambolana Extract was found to improve the effect of oral hypoglycemic medications in Type 2 diabetics who were not well controlled with the medications alone.*

The mechanisms of action of Eugenia jambalona extract include activation of glucose transport, improved glycogen storage, and stimulation of insulin release.28 Laboratory studies support Eugenia jambalona extract ability to improve blood glucose and lipid profiles.31,32

CURCUMINOIDS:
Curcuminoids exerts glucose lowering effect and improvise insulin resistance in Type II Diabetes. This action of Curcuminoids is due to reducing serum free fatty acids (FFAs) and increasing fatty acid oxidation in skeleton muscle. The study has proved that curcuminoids are effective in lowering glucose in blood in type II diabetes.

A highly absorbable curcumin to help maintain healthy inflammatory-mediator levels.*

<table>
<thead>
<tr>
<th>Curcumin: Effects on Aspects of Metabolic Syndrome</th>
</tr>
</thead>
<tbody>
<tr>
<td>↓ Fasting blood sugar*53</td>
</tr>
<tr>
<td>↑ Adipogenesis*54</td>
</tr>
<tr>
<td>↑ Beta-cell function*53</td>
</tr>
<tr>
<td>↓ Leptin → Liver fibrosis in fatty liver*57</td>
</tr>
<tr>
<td>↑ Adiponectin levels*31</td>
</tr>
<tr>
<td>↓ Inflammation in adipocytes*56</td>
</tr>
<tr>
<td>↓ Triglycerides*54</td>
</tr>
<tr>
<td>↑ Insulin sensitivity*51,59</td>
</tr>
<tr>
<td>↑ Circulation*55</td>
</tr>
</tbody>
</table>

Obesity is known to be associated with low levels of inflammation. The inflammation can occur first in the adipocytes, with an increase in TNF-α.6 TNF-α stimulates a more general inflammatory state that can ultimately result in insulin resistance and endothelial dysfunction, which can contribute to hypertension and other vascular complications. Curcumin has been shown to ameliorate many of the inflammatory and metabolic rearrangements associated with metabolic syndrome.33,34

Supplementing with curcumin can benefit patients with pre-diabetes:
In a double-blind, placebo-controlled trial, 240 pre-diabetic patients were given 750 mg curcumin or placebo twice daily for nine months. After nine months, 16.4% of patients in the placebo group, compared to no patients in the curcumin group, had progressed to Type 2 diabetes.

In a study of patients with Type 2 diabetes for at least five years, 37 patients received 500 mg curcumin Twice daily plus standard care, while 38 patients received standard care only (control). After four weeks, Visual activity, peripheral blood flow, and retinal and peripheral edema showed statistically significant improvement in the curcumin group compared to the controls.

Curcumin can benefit patients who have high triglyceride levels:
In a randomized, double-blind trial, 1g/day of Curcumin or placebo was given to obese, non-diabetic patients (n=30) for 30 days. Curcumin was shown to significantly promote normal level of triglycerides.

**Curcumin might have benefits in other obesity-related conditions:**
Several animal and in vitro studies have demonstrated benefits for insulin resistance, adipocyte inflammation, weight management, fat loss, liver fibrosis, and inflammatory response.

**BERBERINE HYDROCHLORIDE**

Berberine is an isoquinolone derivative alkaloid with hypoglycemic effect was first reported in 1998. Berberine showed improved blood glucose control compared with conventional anti diabetic therapy. In addition hypoglycemic effect was enhanced when combined with anti diabetic agent. It also has positive effect on plasma lipid profile in diabetic patients. It also has additional cholesterol lowering effect in treating diabetes. Recent studies have shown this impressive alkaloid has beneficial actions on metabolic activities. As a potent regulator of intracellular metabolism, Berberine affects cellular uptake of glucose, beta-oxidation of fatty acid, insulin sensitivity, and glucose transportation.

Hui Dong, Nanweng, Lizhao, and Fuerfu; No serious adverse side effects except for mild to moderate gastrointestinal disturbances.

**MULBERRY LEAF EXTRACT**

Mulberry leaf extract contains compounds such as fagomines which induces insulin secretion, 


\[ \text{36. J. Nutr 2005; 135: 729-734} \]


\[ \text{Clin Chem Acta 2001; 314: 47-53} \]

\[ \text{37. Int. J. of Food sci. And Nutr, taylao and Francis ltd, 2003;54:411-416.} \]


**Beneficial effects upon ingestion of Mulberry extract**

- Inhibits intestinal Sucrase.
- Induce sucrose malabsorption.
- Reduce microvascular complications of diabetes.

**Change from Fasting Blood Glucose Concentration (mg/dl)**

Influence of mulberry leaf extract on the blood glucose and breath hydrogen response to ingestion of 75g sucrose by subjects with Type 2 diabetes and controls.

Changes in blood glucose concentration from the fasting concentration of 10 healthy controls (upper panel (A)) and 10 subjects with Type 2 diabetes (lower panel (B)) after ingestion of 75g sucrose with 1.0g of Mulberry leaf extract (white squares) or placebo (black circles). The significance of difference between mulberry leaf extract and placebo over the first 120 minutes of the study, determined by ANOVA, was highly significant for controls (p=0.0050 and subjects with diabetes (p=0.002).
CYNARINS FROM ARTHICHOKE LEAF EXTRACT:
Arthichoke is a plant. The leaf, stem, and roots are used to make 'Extract' which contains a higher concentration of certain chemicals found in the plant. These extracts are used as medicine Cynara Scolymus (Artichoke) acts as lowering glycemic effect. Clinical studies have proven that Cynara Scolymus is capable of lowering post-prandial glycaemia. It has been shown to help maintain healthy glucose and cholesterol levels in obese individuals. It also provides support for healthy bile flow and liver function.


COROSOLIC ACID from BANABA LEAF EXTRACT
Corosolic acid impacts glucose parameters of Type 2 diabetes by way of insulin like activity, stimulating glucose uptake by body cells and inhibiting adipocyte differentiation. The corosolic acid in banana leaf extract has been shown to stimulate glucose transport activity and significantly aids in regulation of blood sugar levels. It helps to lower serum insulin, urinary excreted glucose and total plasma cholesterol. It is said to have a memory effect of blood glucose lowering even after intake is stopped, confirmed safe and effective by the clinical studies.

42. Hayashi T, et al Planta med 2002; Feb68(2), 173-5

L-GLUTATHIONE:
Glutathione is a tripeptide Synthase from glutamate cysteine, sustained hyperglycemia is associated with lower cellular levels of the antioxidants glutathione, which leads to tissue damage attributed to oxidative stress. Glutathione exerts Glycemic control which diminishes the incidence of diabetic microvascular complications by decreasing oxidative stress.

CHARATIN FROM BITTER MELON EXTRACT:
Momordica Charantia is a fruit used for the Treatment of diabetes and related conditions. It has a significant anti diabetic, and Hypolipodemic activity so that it can be used as adjuvant therapy along with allopathic medicine Studies has reported that 'Charatin' a typical 'curditane type triterpenoid in M. Chantin is more effective than other hypoglycemic agents tolbutamine. (Cousens G. North Atlantic book, 2008.)

It shows hypoglycemic effect by stimulation of peripheral and skeletal muscle glucose utilization. (Cummings E Hundal, MS, Wackerhage H, etal), inhibition of intestinal glucose uptake (VebansoT, Arai H, Taketaniy etal 2007), Inhibition of adipocyte differentiation (NerukarPV, Lee YK Nerukar Med 2010; 10.34), Suppression of key gluconeogenic enzymes, preservation of islet Beta cells and their functions (Gadang V, Gilbertw, Hettiara, rehylhy N, Horax R, Katwal, Devareddy).

GYNEMIC ACIDS FROM GYMNEMA SYLVESTRE EXTRACTS
Gymnema Sylvestre(Sugar Killer) is a medicinal Plant that grows in the open forest of India, China, Indonesia, Japan, Malaysia, Sri Lanka and South Africa. The leaves of these plants are used as Antiallergic, Hypoglycemic, and Hypolipidimic. (Saneja.et.al.2010) The studies have showed that the Gymnemic Sylvestra extract, significantly decreases the plasma glucose level, it controlled gluconeogenic levels in Liver, kidney and muscles (Shanmugasundaram.et.al.1990). It has a direct effect of increase in insulin level up to 50% (Bolkent et.al.2000, chattopadhay (1998). This extract showed significant decrease in triglyceride, cholesterol and LDL cholesterol and increase in the level of HDL Cholesterol, due to increase in Insulin which resulted in increased activity of Lipoproteins Lipase.(Daisy et.al.2009) Studies showed that G.Slvestre leaves treats complications like Hyperglycemia, Hyper insulinemia, Hyperlipidemia and Oxidative stress.

Ref : Aziza A.M. EL shafey, Magda M.EL DOI : 10.1016/JJ KSUS.2012.11.001

Rajagopal Vsekar MD, V Mckay, MD and Farooil Jahooor Phd
Diabetic Care, Jan2011; 34(1): 162- 167
METHYL HYDROXY CHALCONE POLYMERS FROM CINNAMON EXTRACT

Aqueous extracts of cinnamon have been shown to increase in vitro glucose uptake, glycogen synthesis, phosphorylation of insulin receptors and aids in trigerring the insulin cascade system. A novel MHCP was identified, which increases the glucose metabolism of the cells 20 fold in vitro in the epididymal fat cell assay. The MHCP in cinnamon strongly inhibits the formation of reactive oxygen species in collagen-activated platelets in vitro so may provide synergistic benefits. Cinnamon also contains procynadin dimmers and oligomers of the type thought to improve capillary function.

MHCP AND INSULIN HAVE SYNERGISTIC EFFECT

We have isolated and characterised the active constituents from cinnamon and shown that they are type A polymers (A type doubly linked procynadin polymers of the catechins and/or epicatechins, with a molecular weight of 864 and 1152 respectively (few studies show type A polymers as MHCP). These complexes not only improve insulin function but also work as antioxidants in Ferric reducing antioxidant power (FRAP) assay and in prevention of copper induced LDL oxidation. Type A polymers potentiates insulin activity and also inhibits insulin receptor phophatase activity, thus mimics the action of insulin induced signalling via its receptor. Cinnamon extracts have been shown to positively affect numerous aspects of MetS in individuals with obesity, pre-diabetes, diabetes, or PCOS (Table 3). In one study using specifically the cinnamon extract, supplementation of 6.25 mg twice daily or placebo for two months to 137 individuals with Type 2 diabetes significantly improved fasting and postprandial glucose levels in the cinnamon group.

MHCP in Insulike

The polyphenol type A polymers from cinnamon up regulates expression of genes involved in activation & phosphorylation of insulin receptor and increase glucose uptake in cell studies, other cinnamon polyphenols such as MHCP have been shown to be potent insulin mimetic. MHCP / Type A Polymers mimics insulin, activates its receptors and works synergistically with insulin in the cells.

Cinnamon extracts have been shown to positively affect numerous aspects of MetS in individuals with obesity, pre-diabetes, diabetes, or PCOS (Table 3). In one study using specifically the cinnamon extract, supplementation of 6.25 mg twice daily or placebo for two months to 137 individuals with Type 2 diabetes significantly improved fasting and postprandial glucose levels in the cinnamon group. Each serving of INSULIKE contains 6.25 mg of Cinnamon extract.

MHCP in cinnamon extract shows positive affects of several aspects of metabolic syndrome in individuals with obesity, including maintenance of healthy blood sugar, lipids, and lean muscle mass.

### Table 3. Beneficial Effects of Cinnamon

<table>
<thead>
<tr>
<th>Effect</th>
<th>Cinnamon (6.25 mg)</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin sensitivity</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Glucose transport</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Hemoglobin A1c (HbA1c)</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Inflammation</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Blood pressure</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Oxidative stress</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Vascular endothelial growth factor to decrease adipogenesis</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Formation of advanced glycedated end products (AGEs)</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Percent body fat</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Fasting blood sugar</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Lean muscle mass</td>
<td>↑</td>
<td>↓</td>
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<tr>
<td>HDL-cholesterol</td>
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</tr>
<tr>
<td>LDL-cholesterol</td>
<td>↑</td>
<td>↓</td>
</tr>
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44. Impart rodosevich J, Deas S, Polansky, MM Beedleke DA, IngerbrustenTS Anderson RA, Graves DJ; regulation of phosphorylase phophatase (PTP-1) and insulin receptor kinase by fractions from cinnamon; implications from Cinnamon regulation of insulin signaling. Horm res 50; 177-182, 1998.
**4 HYDROXY ISOLEUCINE FROM FENUGREEK EXTRACT**

The fraction of fenugreek that contains the testa (i.e., the portion and the endosperm of the defatted seeds (i.e., the subfraction are thought to be associated with the hypoglycemic effects of fenugreek, these effects have not been observed in the studies of lipid extracts and the extract used in INSULIKE is water extract. It is possible fenugreek lowers lipids because it contains 50% fiber (30% soluble fiber and 20% insoluble fiber) that can slow the post prandial glucose absorption. This may be a secondary mechanism for its hypoglycemic effect.

The hypoglycemic effects of fenugreek have been attributed to several mechanisms, (savior et al) in vitro studies demonstrated that the amino acid 4 hydroxy isoleucine in fenugreek extract increased glucose induced insulin release in human and rat pancreatic islets. The amino acid appeared to act only on pancreatic beta cells, since the levels of somatostatin and glucagons were not altered. In human studies, fenugreek reduced the area under the plasma, glucose curve and increased the number of insulin receptors, although the mechanism of this effects is unclear. In humans, fenugreek extract exerts hypoglycemic effects by stimulating glucose dependent insulin secretion from pancreatic beta cells, as well as by inhibiting the activities of alpha amyrase and sucrase, two intestinal enzymes in carbohydrate metabolism.

---

**TABLE**

**Safety : A review of literature of fenugreek reveals.**

<table>
<thead>
<tr>
<th>Condition Treated (Primary or Secondary Outcome)</th>
<th>Evidence/Study Type</th>
<th>Author, Year Reference</th>
<th>N</th>
<th>Statistically Significant Results</th>
<th>Magnitude of Benefit (how strong is the effect)</th>
<th>Absolute Risk Reduction</th>
<th>Number of Patients Needed to Treat for One Outcome</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes, hyperlipidemia</td>
<td>Randomized, controlled, double-blind study</td>
<td>Gupta 2001 J.Assoc Physicians India 2001;49: 1057-1061</td>
<td>25</td>
<td>Yes</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Improved fasting glucose &amp; GGT with fenugreek seeds or diet/exercise, without differences between groups. Altered AUC &amp; insulin resistance with fenugreek.</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Randomized, crossover study</td>
<td>Raghuram TC Phytother Res 1994;6:83-86</td>
<td>10</td>
<td>Yes</td>
<td>Large</td>
<td>NA</td>
<td>NA</td>
<td>Improved peripheral glucose utilization with fenugreek seed supplementation</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Randomized, crossover study</td>
<td>Sharma 1990 Nutr Res 1990; 10:731-739</td>
<td>15</td>
<td>Yes</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>Improvement in reported diabetic symptoms</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>Case series with matched controls</td>
<td>Neeraja 1996 J.Food Sci Technol 1996; 33:427-430</td>
<td>12</td>
<td>Yes</td>
<td>Medium</td>
<td>NA</td>
<td>NA</td>
<td>Improvement of acute glycemic response, most notable with raw fenugreek seed powder</td>
</tr>
<tr>
<td>Type 1 diabetes hyperlipidemia</td>
<td>Randomized, crossover study</td>
<td>Sharma 1990 Eur J.Clin Nutr 1990;44:301-306</td>
<td>10</td>
<td>Yes</td>
<td>Large</td>
<td>NA</td>
<td>NA</td>
<td>Fasting blood glucose levels and GGT improved: serum insulin levels unchanged</td>
</tr>
</tbody>
</table>
ANTHOCYANINS FROM BILBERRY FRUIT EXTRACT

Vaccinium Myrtillus (bilberry or European blue berry) is a shrub plant that grows in Europe. The anthocynosides and chlorogenic acid being the most important constituents. Bilberry has been shown to beneficially effect in micro vascular abnormalities of diabetes. It has also been shown to improve edema and microangiopathy.65,66.

EGCG (Epigallocatechin gallate From Green Tea Extract)

EGCG inhibits cytokines responsible for destruction of pancreatic beta cells in Type 1 diabetes. It also inhibits the enzyme action to suppress glucose production, suppress the uptake of glucose by the intestine and enhances insulin activity. It also protects from oxidative damage.

CHROMIUM PICOLINATE

A major detriment of insulin sensitivity, as it functions as a cofactor in all the insulin regulating activities. Chromium facilitates insulin binding and subsequent uptake of glucose into the cell. Supplemental chromium has been shown to decrease fasting glucose levels, improve glucose tolerance, lower insulin levels and decrease total cholesterol and triglycerides, while increasing HDL cholesterol in normal, elderly and Type 2 diabetes subjects without blocking insulin action. Chromium picolinate has been well studied for its beneficial effects on insulin resistance and diabetes. A 2004 review found the mineral enhanced glucose uptake and glycogen synthesis, in addition to improving insulin function. A 2004 clinical trial concluded chromium picolinate had an acute effect on the post prandial glucose metabolism in young men, possible lowering glycemic index of a meal. A 2002 trial found the mineral improved glucose control by enhancing insulin action rather than secretion. While Israeli researchers demonstrated 200 mcg/day of chromium picolinate balanced glucose levels and reduced serum lipid levels. A result verified by dutch researchers at an even higher dose of 1000 mcg/day. Animal trials have shown similar results, showing chromium picolinate supplementation can lower glucose levels and improve insulin sensitivity in rats, as well as lower fasting insulin levels and glucose disappearance in hyper insulinenia. Chromium provides support for healthy glucose metabolism and helps the body metabolize carbohydrates and fats.

Chromium supplementation has been reported in clinical trials for over five decades to improve insulin regulation and glucose tolerance. In a meta-analysis of 41 studies, chromium was shown to significantly improve fasting glucose and HbA1c levels in Type 2 diabetics. A meta-analysis of 11 studies found chromium supplementation compared to placebo resulted in significant decreases in body weight and percent body fat.
SELENIUM:
Selenium is a mineral found in soil plays a key role in Metabolism. Selenium is found to have action similar to Insulin like molecule for the down regulation of glucose level. The case studies on diabetes subjects stated that: Selenium treatment induces insulin like effects in lowering Serum glucose level and it also significantly decreases serum biochemical components associated with liver damage and lipid metabolism. Its treatment also reveals Apoptosis of Liver tissues. It is concluded from the clinical studies that Selenium lowers serum glucose and biochemical profiles associated with liver damage and lipid metabolism in diabetes.

VITAMIN D3:
Vitamin D deficiency has been shown to alter insulin synthesis and secretion in both humans and animal models. Vitamin D supplementation improves glycemia and insulin secretion in patients with Type II diabetes with established hypovitaminosis. The mechanism of action of Vitamin D in type II Diabetes is by mediating not only through regulation of Plasma Calcium level, which regulates Insulin Synthesis but also through the direct action on pancreatic beta cell function.

MAGNESIUM:
Magnesium is a chemical element and an alkaline earth metal and most abundant ion present in the living cells and its plasma concentration is remarkably constant in healthy subjects. Intracellular magnesium concentration is highly regulated by several factors among them insulin seems to be most important. In vitro and invivo studies have demonstrated that the insulin may modulate the shift of magnesium from extracellular to intracellular. Intracellular magnesium concentration has also been shown to be effective in modulating insulin action (mainly oxidative glucose metabolism), calcium related excitation concentration coupling and decreases smoothly. From the studies it is concluded that intracellular magnesium may play a key role in modulating insulin-mediated glucose uptake and vascular tone.

METHYLCOBALAMINE:
Methylcobalamin has a potential benefit in treating Diabetic Neuropathy. Low levels of Vitamin B 12 often lead to diabetic Neuropathy with high levels of blood vessels damaging compound homocysteine (Fahmy 2010). Vitamin B 12 also known as Methylcobalamine has high affinity for nerve tissue (Mizukami 2011) studies on animal models of diabetic neuropathy has found that methycobalamine may mitigate the damage caused by diabetic. Neuropathy possibly by modulating protein kinaseC' signaling pathways or activating chemical signals that helps nerve survive.

VITAMIN C
Vitamin C is known to inhibit the process of glycation to some degree, thus helping to prevent the tissue Glycencing effect of those AGE'S, it also improves lipid metabolism. Vitamin C is known to inhibit the accumulation of sorbitol, a sweet tasting alchol derived from glucose, excess sorbitol is implicated in the formation of cataracts in diabetic individuals and it is thought to lead to diabetic neuropathy, a cathall term that means a functional disturbance or pathological change in the pheripheral nervous system. Diabetic neuropathy is common in the early stages of Type 1 diabetes and also in the later stages of Type 2 diabetes.

VITAMIN E
Vitamin E has been shown to reduce glycosylation of tissues. Vitamin E enhances immunity and reduces the number of infections with higher plasma vitamin E levels. Alpha tocopherol was found to decrease both C-reactive protein and cytokine interleukin-6 in normal volunteers and Type 2 diabetic patients. Vitamin E works synergistically with other nutrients to protect against the nerve and kidney damage.

Also supplementation of Vitamin E resulted in the decrease in both glucose disposal rate and number of insulin receptors on erythrocytes. Also reported an improvement in insulin sensitivity in hypertensive patients.

**VITAMIN K**

Vitamin K in the form of phylloquinone, the form found in plants and leafy vegetables, although deficiencies of this vitamin are rare it is included for good measure because Japanese researchers have found that it can help improve insulin sensitivity and blood sugar regulation.

**VANADIUM**

Prior to the discovery of insulin in 1922, vanadium was used for the control of blood sugar. Two small studies (one with six type 2 diabetic patients; one with seven type 2 diabetes patients) have confirmed the effectiveness of vanadyl sulphate in improving insulin sensitivity.

Vanadium has also shown some overall blood glucose lowering ability. As well as an ability to effectively control altered glucose metabolism and antioxidant status in diabetic rat lenses.


**BIOTIN**

Biotin helps to lower post prandial glucose levels, improved response to a glucose load & decreased insulin resistance. This vitamin has demonstrated an ability to improve glucose metabolism in human dialysis with Type 2 diabetes.

89. Icotitsikos, D, Fourtounas C, kapetanaki A, et.al, oral glucose tolerance test after high dose i.v. biotin administration is normoglucemic hemodialysis patients. Ren.Fail. 1996;18:131-137.

**ACETYLC YSTEINE**

Acetylcysteine is an approved nutraceutical and it is essential branched chain aliphatic amino acid found in many proteins. It is important in hemoglobin synthesis and regulation of blood sugar and energy levels. Clinical studies on normal and diabetic subjects concluded that the both acute and chronic treatment with acetylcysteine is beneficial for glucose metabolism and glucose intolerance.

Isoleucine is a branched-chain amino acid. Like exercise, isoleucine has been shown to enhance uptake of glucose by skeletal muscles and decreases glucose production in the liver. Branched-chain amino acids can also help reduce fatigue during exercise.

84,85

**ISOLEUCINE:**

Isoleucine is a branched-chain amino acid. Like exercise, isoleucine has been shown to enhance uptake of glucose by skeletal muscles and decreases glucose production in the liver. Branched-chain amino acids can also help reduce fatigue during exercise.

84,85

**GLYCINE:**

Glycine is an amino acid. This is shown to stimulate secretion and decrease glycated hemoglobin in Type II diabetes. Treatment with glycine is likely to have a beneficial effect on innate and adaptive immune responses and may help prevent tissue damage caused by chronic inflammation in patients with Type II diabetes. It has been shown to increase adiponectin, which can down-regulate inflammatory cytokines in fat tissue, thus helping to modulate inflammation associated with obesity and MetS.

87,88

**BIOTIN**

Biotin helps to lower post prandial glucose levels, improved response to a glucose load & decreased insulin resistance. This vitamin has demonstrated an ability to improve glucose metabolism in human dialysis with Type 2 diabetes.

89. Icotitsikos, D, Fourtounas C, kapetanaki A, et.al, oral glucose tolerance test after high dose i.v. biotin administration is normoglucemic hemodialysis patients. Ren.Fail. 1996;18:131-137.

**BENEFOTAMINE:**

It is a fat soluble derivative of thiamine that is more readily absorbed by digestive tract (SancheZ - RamireZ 2006). It modulates several pathways that contribute to Diabetic Neuropathy: The Formation of AGEs, the protein kinase ‘C’ pathways and damaging changes that occurs within cells due to high glucose level ( Varkonyi 2008, Balakumar 2010). It also helps to prevents vascular problem. (Stracke 2008). It improves carbohydrate and amino acid metabolism to produce cellular energy. It has found to be neuro and nephroprotective in situations associated with elevated blood sugar.

CONCLUSION & FUTURE DIRECTION

The incidence of Type 2 diabetes is increasing dramatically worldwide, resulting in large measure from the increasing prevalence of obesity. In addition, research is uncovering the importance of “Pre-diabetic” state or metabolic syndrome, when insulin resistance gives rise to impairment of glucose metabolism. Unfortunately, patients who have metabolic syndrome or diabetes are at greatly increased risk of cardiovascular morbidity and mortality. Thus, Insulike approach can modulate glucose homeostasis and potentially improve lipid parameters, which would be desirable. This is especially true for diabetes prevention in patients with metabolic syndrome. These patients already manifest abnormalities of glucose handling and could be relief from a low-risk, in expressive, food based intervention aimed at normalizing their metabolic milieu. Insulike as a dietary supplement that may hold promise in this regard. The data generated to date are sparse but will hopefully help to the development of well designed adequately powered, randomized, clinical trials evaluating the effect of Insulike on measures of insulin resistances, insulin secretion, insulin binding, sensitivity glucose absorption & cholesterol metabolism.

ORTHOMOLECULAR MEDICINE:
VISIONARY SCIENCE

In 1968, the Noble Prize-winning scientist Linus Pauling, PhD, published an article in the journal Science describing “orthomolecular” approach to illness. This was the first time that such an approach was presented to the public specifying that “varying the concentration of substances normally present in the human body may control mental disease.” Dr. Pauling later extended this strategy beyond mental illness to include the discipline of orthomolecular medicine.

Orthomolecular medicine is a paradigm that attempts to prevent and treat disease by integrating conventional medicine therapies with vitamins, phytonutrients, and other dietary micronutrients.

PHENOTYPIC NUTRITION A NEW STRATEGY FOR PREVENTING METABOLIC SYNDROME

A powerful strategy called phenotypic nutrition can help modulate the expression of your unique code, thus dramatically reducing your risk of developing disease. Phenotypic nutrition uses specific nutrients with the biochemical and genetic effects to help protect you from disease.

One of the most important threats to your health and longevity is metabolic syndrome, a disorder little known to the fast becoming an extremely important public health issue. This deadly, common condition affects approximately one in five people overall, with even higher rates among certain ethnic groups. By applying a phenotypic nutrition strategy, we can help to guard against the deadly dangers of cardiovascular disease associated with metabolic syndrome.

NUTRIGENOMICS: GUIDING GENETIC DESTINY

Driven by the recent technological breakthroughs associated with the mapping of the genome, the science of nutrigenomics holds great potential for predicting how specific nutrients and dietary ingredients can directly affect the disease by specific genetic interactions. Nutrigenomics holds promise in advancing the goal of preventing diseases with “individualized nutrition” based on unique genetic needs. Currently, however, nutrigenomics remains a very young and developing science that has not yet developed to the potential of being able to offer broad-based nutrient-gene testing of this sort. There is, however, another approach that we can use for specific, individualized nutrient recommendations that incorporate Dr. Pauling's visionary approach to orthomolecular medicine. This alternative approach is called phenotypic nutrition.
GENES, GENOTYPE, AND PHENOTYPE

Your unique genetic code defines your genotype. The expression of your individual genetic code is your phenotype. Your genes and your environment influence your phenotype.

While it is not known exactly which genes are responsible for the constellation of abnormalities associated with metabolism syndrome, a number of genes so far identified play a role in the malfunction associated with abnormally elevated plasma glucose.

Metabolic syndrome is a phenotypic expression of the genetic code as it interacts with the environment. Specifically, have a genetic tendency to develop the metabolic syndrome phenotype, you will be far more likely to develop this phenotype if you are overweight, do not exercise, consume a diet high in simple sugars and saturated fats, and do not consume specific nutrients with beneficial nutrient-gene interactions.

In 2004, an innovative approach to weight management and obesity was published in the peer-reviewed journal Curr. Ther. Targets. This approach called “nutriphenotypic,” is selective nutrition based on an individual's phenotypic metabolic characteristics.

This past year, researchers described the concept of a “nutritional phenotype” that characterizes the relationship of biochemical measures, metabolic parameters, and functional characteristics (for example, exercise, body weight, example to environmental pollutants and toxins, emotional stress) on health. The nutrient phenotype is a function of genes, disease environment, and behavior.

The nutriphenotypic/nutrient phenotype approach represents an integrative strategy to help prevent and treat disease just as specific inputs to a computer will cause specific outputs, phenotypic nutrition uses specific nutrients for specific effects.

Phenotypic nutrition affects the expression of your genes and unique biochemistry so that you can influence your genetic destiny. Instead of dooming individuals to disease and an early demise due to “bad genes,” phenotypic nutrition uses nutrients that act on specific genes as well as biochemical and molecular pathways to help prevent disease and achieve optimal health and longevity.

With phenotypic nutrition, once high-risk individuals have been identified, strategies that include dietary modifications and supplementation of specific nutraceuticals can be implemented to help decrease disease risk.

Identifying Those Most AT Risk

Metabolic syndrome is characterized by insulin resistance. Identifying individuals with evidence of insulin resistance the development of full-blown metabolic syndrome allows us to intervene with a nutrient and lifestyle strategy to prevent progression of this condition.

Thankfully, simple metabolic markers are very useful in helping to identify individuals with insulin resistance who are at risk of cardiovascular disease.

Triglycerides, Insulin, and HDL. Clinical studies suggest that the following Threshold values for plasma triglycerides ratio of triglycerides to HDL, and fasting insulin are the most useful metabolic markers in identifying insulin-resistant individuals at risk of cardiovascular disease.

Triglycerides greater than or equal to 130 mg/dL,
Triglycerides/HDL ratio greater than or equal to 3.0,
Fasting insulin level greater than or equal to 15 µU/mL,
C-reactive protein

Moreover, research has demonstrated that a condition of low-grade systemic inflammation is associated with insulin resistance. For example, a recent clinical study showed that insulin and insulin resistance remained significantly and independently related to C-reactive protein (CRP) levels, a marker of inflammation, after adjustments for age, sex, body mass index, waist size, alcohol consumption, level of physical activity, and smoking habits. Another clinical study that CRP was significantly correlated to insulin resistance.

LIPOIC ACID

A naturally occurring nutrient, lipoic acid is known to improve glucose metabolism by influencing genetic transcription factors in fat cells through the mitogen-activated protein kinase (MARK) pathway. For example, in a multicenter, p controlled trial, type II diabetes patients treated with lipoic acid demonstrated a significant increase in insulin-stimulate glucose disposal. Furthermore, lipoic acid's molecular attributes include increasing glucose uptake through recruit the glucose transporter-4 (GLUT-4) to plasma membranes, a mechanism that is shared with insulin-stimulated glucose uptake.
Research also shows that lipoic acid decreases markers of vascular inflammation in metabolic syndrome. A recent randomized, double-blind clinical trial showed that after four weeks of therapy, endothelium-dependent vasodilatation of bronchial artery was increased by 67%, 44%, and 75% in groups receiving irbesartan (an angiotensin-blocking drug), lipoic acid, and irbesartan plus lipoic acid, respectively, compared to placebo. Furthermore, treatment with irbesartan and lipoic acid was associated with statistically significant reductions in plasma levels of pro-inflammatory mediators such as interleukin\^106.

**CINNAMON EXTRACTS**

In clinical trials, cinnamon has demonstrated remarkable effects on glucose control.

In 2003, a placebo-controlled study of Type 2 diabetes patients who were given one, three, or six grams a day of cinnamon placebo showed that after 40 days, all three levels of cinnamon reduced mean fasting serum glucose by 18-29%, Triglycerides by 23-30%, LDL by 7-27%, and Total Cholesterol by 12-26%. No significant changes were noted in the other groups\^112.

Cinnamon also has been shown to have excellent antioxidant properties. Natural water-soluble cinnamon extract (as in Insulike Tablets) has shown to inhibit oxidation by 88%, while a synthetic antioxidant control, butylated hydroxytoluene, inhibited oxidation 80%\^113.

Water-soluble polyphenol polymers (polyphenol type-A polymers) from cinnamon increase insulin-dependent glucose metabolism in vitro. These polymers have recently been characterized by nuclear magnetic resonance and mass spectroscopy\^114.

The polyphenol Type-A polymers from cinnamon up-regulate expression of genes involved in activation of (phosphorylation) the insulin receptor and increase glucose uptake in cell studies\^115. In other cinnamon polyphenol such as methylhydroxychalcone have been shown to be potent insulin mimics\^116.

**BIOFLAVONOIDS GREEN TEA EXTRACT**

Inflammation and associated insulin resistance play a critical role in the development of metabolic syndrome and Type of diabetes\^107,108. Nutrients that act to down-regulate genes involved in inflammation are critical to preventing metabolic syndrome.

**TOCOPHEROLS**

Vitamin E is an important nutrient in preventing metabolic syndrome, as it helps regulate several genes affecting cardiovascular disease risk\^109.

Genes that are associated with lipid uptake and Atherosclerosis (CD36, SR-BI, and SR-AI) Genes that are related to inflammation, Cell adhesion, and platelet aggregation (E-Selection, ICAM-1, integrins, glycoprotein IIb, IL-2, IL-4, and IL-beta).

Furthermore the appropriate genetic regulation of glucose transport protein (GLUT-3) is critical to optimal blood glucose control. Studies have shown that both aging and vitamin E deficiency are associated with decreased expression of Glut-3\^110.

**VITAMIN C**

Using data from the Third National Health and Nutrition Examination Survey (1988-1994), researchers evaluated the levels of vitamins A and C, retinyl esters, five carotenoids and other trace nutrients in 8,808 US adults aged 20 and older without metabolic syndrome. After adjusting for factors like age, sex, ethnicity, education smoking status and physical activity they found that individuals with metabolic syndrome had significantly lower concentrations of retinyl esters, Vitamin C and carotenoids except lycopene\^111.
**Lactonova** goes a step further to steer patients toward low-carbohydrate foods and away from common food allergens that can contribute to inflammation.

**Benefits of Exercise & Stress Management**

**Exercise**

The benefits of exercise are well known and accepted. In weight-loss programs exercise enhances maintenance of lean muscle mass. Lean muscle tissue assists in utilization of glucose and improves fatty acid metabolism. Citation of several studies helps illustrate specific benefits. For example, a 12-week exercise regimen consisting of 80 minutes of mixed aerobic and resistance training three days a week by Korean college students resulted in a significant reduction in percent body fat, waist circumference, and blood pressure.

Exercise by older adults with metabolic syndrome had a positive effect on blood pressure, Triglycerides, HDL-cholesterol levels, Waist Circumference, body composition, aerobic fitness, and insulin resistance. The participants exercised 60 minutes a day, five days a week, regardless of whether they were following a high- or low-glycemic index diet.

Other studies illustrate the benefit of coupling exercise with dietary modifications. Research on pre-diabetics found a low-glycemic index diet partnered with exercise adds additional protection by lowering postprandial hyperinsulinemia and preserving pancreatic beta-cell function when compared to a high-glycemic index diet.

In addition to nutritional and dietary interventions, prevention and correction of MetS should focus on increasing fitness levels for all age groups (see Metabolic Syndrome Patient Guide for specific exercise tips).

**Reducing Stress**

There is a strong connection between elevated cortisol levels and elevated blood sugar, hyperinsulinemia, and obesity. Exercise is a good way to reduce the effects of stress. Yoga exercise, for instance, can decrease salivary cortisol levels, increase GABA (an inhibitory neurotransmitter involved in relaxation), and result in improvements in mood and anxiety. In one study, both 60-minute yoga and 60-minute walking were shown to improve GABA levels, as well as feelings of anxiety, although yoga was more effective than walking.

Although cortisol can become elevated during periods of extreme exercise (such as marathons), jogging can result in a decrease in stress hormones. One study of 18- to 20-year old females found 50 minutes of jogging five days per week resulted in decreased urinary output of the stress hormones epinephrine and cortisol. Jogging also resulted in improvements in depression.

**Testing Salivary**

**Cortisol Levels**

Salivary cortisol is a reliable and simple means to assess cortisol levels in patients, and the kits can be provided by many labs. The test requires merely that a patient collect saliva in a test tube four times daily—At 8 AM, noon, 4 PM, and 11 PM. The samples are mailed back to the lab. Other hormones, such as DHEA, Testosterone, and Estrogens, can be measured in this way as well.

**BENEFITS OF SLOW RELEASE FORMULATIONS:**

Slow release drug delivery system optimizes the biopharmaceutical, pharmacokinetic and pharmacodynamic properties of a drug in such a way that its utility is maximized, side effects are reduced and cure or control of the condition is achieved, in the shortest possible time by using smallest quantity of drug administered by the most suitable route. Slow release drug formulations have become more important in therapy as a means of reduced dosing frequency, hence potentially improving patient compliance and consequently efficacy. The efficient benefits of slow release formulation include:

- Decreased dose frequency
- Reduced peak to through ratio of drug in systemic circulation
- Reduced rate of rise of drug concentration in blood
- Sustained and consistent blood level within the therapeutic window
- Enhanced bioavailability
- Reduced side effects
- Improved patient compliance

**CONCLUSION**

Phenotypic Nutrition enables you to choose dietary strategies and nutrients that influence powerful biochemical and factors to help control the expression of your genetic code to your benefit.
Super Natural Sugar Balance

Insulike™
A Nutriphenotypic Approach

Supplement Facts

<table>
<thead>
<tr>
<th>Serving size</th>
<th>1 Tablet</th>
<th>Servings per pack: 100</th>
</tr>
</thead>
</table>

Each film coated tablet contains:

- Eugenia Jambolana extract: 100mg
- Curcuminoids: 50mg
- Berberine Hydrochloride: 50mg
- Mulberry leaf extract 4:1: 30.5mg
- Synamos: 5mg
- from Artichoke leaf extract
- Baana leaf extract: 12mg
- L-Glutathione: 2.5mg
- Gymnemic acids: 10mg
- from Gymnema sylvestre extract
- Charantin: 10mg
- from Bitter melon extract
- Methyl hydroxy chalcone polymers: 6.25mg
- from Cinnamon extract
- 4-Hydroxy isoleucine: 1.25mg
- from Fenugreek
- Anthocyanins: 3.10mg
- from Bilberry fruit extract

Epigallocatechin gallate (EGCG): 10mg
from Green tea extract

Alpha-lipoic acid: 100mg
Chromium (as Chromium picolinate): 40mcg
Selenium (as L-Selenomethionine): 55mcg
Magnesium: 40mg
Vitamin C: 40mg
Vitamin E: 12mg
Vitamin K: 30mcg
Vanadium: 1mg
Biotin: 50mcg
Benfotiamine: 25mg
Inositol: 25mg
Glycine: 25mg
N-acetyl cysteine: 25mg

For further info:

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