

APPRESS

MONOGRAPH



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APPRESS™ *(Glucapress PCL™)*

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Introduction

Losing weight, maintaining an optimal body weight, and serum glucose control are closely linked. Energy levels, mood swings and overall health are related to serum glucose control as well. This monograph details information on the enormous and rapidly increasing problems known by a variety of labels including insulin resistance, impaired glucose tolerance, “pre-diabetes”, Metabolic Syndrome and Syndrome X. The monograph explores the relationship of the above condition with the problem of being overweight, a problem that has reached epidemic proportions in today’s society. A summary of a triple-blinded, randomized, placebo controlled study of **APPRESS™** is presented. Finally, evidence-based outcomes and scientific studies of phytotherapeutic components of **APPRESS™** are discussed.

Scope of the Problem

Resistance to the activity of the hormone insulin is a widespread problem. It is responsible for a host of known problems and will likely be found linked to many more as our understanding of the condition progresses. Increased appetite, weight gain, elevated blood glucose levels, mood swings, decreased energy and a resistance to weight loss are just some of the difficulties caused by insulin resistance¹. Difficulty with weight loss is a common theme in those with insulin resistance. The number of individuals with weight problems is readily evident in our culture. An article published in the Journal of the American Medical Association found that 65% of Americans are overweight². The number of people with pre-diabetes or impaired glucose tolerance is 17 million³ and it is estimated that 22% of the adult population has syndrome X. People are struggling with this- Americans spend over \$33 billion annually on weight-loss services⁴- but are not making headway and in fact seem to be getting more overweight with each passing year.



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What is Pre-Diabetes, Insulin Resistance, Syndrome X, the Metabolic Syndrome?

Pre-Diabetes is a condition in which blood glucose levels are higher than normal but not yet diabetic. *Syndrome X*, the *Metabolic Syndrome* and *Insulin Resistance Syndrome* are often used interchangeably. The term Syndrome X was coined in 1988 by an endocrinologist. The hallmarks which distinguish it had been known prior to that date as the metabolic syndrome or insulin resistance syndrome. Originally Syndrome X was characterized by four findings—abdominal obesity, high triglycerides and low high-density lipoproteins, high blood pressure, and insulin resistance. It is the insulin resistance that underlies much of the problem seen in the syndrome. Being overweight is believed to be one of the factors which may predispose an individual to experience any of the above mentioned findings

The modern diet puts a tremendous strain on the glucose-insulin system. The body is chronically exposed to high serum glucose levels. Our more sedentary lives do not require the amount of energy supplied by our diets. In response to this higher serum glucose level, the pancreas secretes ever increasing amounts of insulin. Eventually, higher insulin levels overcome the number on insulin receptors found on the cells. This is the condition of “*insulin resistance*”. The cells are relatively resistant to the effect of insulin and so both the serum glucose level and the insulin level remain elevated. Over time this can have numerous negative effects upon the body.

Why is serum glucose control important?

When the glucose level in the bloodstream remains higher than the normal range, problems begin to develop. Firstly, the cells of the body do not get the energy they need, since more of the glucose remains in the blood. Secondly, over time, high serum glucose levels can lead to damage to blood vessels, nerves, the immune system, eyes and kidneys, among other organs. The longer the serum glucose levels stay elevated, the greater the chances of damage occurring. Blood vessels can develop blockages and become thicker and less flexible, leading to difficulties with circulation and wound healing. If decreased blood flow occurs in organs such as the heart or brain, stroke or heart attacks may happen. Circulation problems can also contribute to erectile dysfunction and sexual difficulties. Nerve problems from prolonged high serum glucose may involve decreased feelings in parts of the body, or painful pins and needles type sensations. In the eye, problems with the small blood vessels in the retina can lead to impaired vision and even blindness. In the kidneys, prolonged damage to the blood vessels there can develop into kidney damage and can even eventually lead to the requirement for dialysis. Weight loss can be extremely difficult in the face of widely fluctuating serum glucose levels. While the exact mechanism of what we feel as “hunger” is an interplay of a variety of factors, large peaks and valleys in serum glucose levels can make it extremely difficult to lose and maintain significant weight loss.



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How does the body process and regulate glucose?

All of the food we eat is broken down in our stomachs and intestines into basic nutrients- this is the process of digestion. The carbohydrates and proteins we eat are broken down through mechanical, chemical and enzymatic processes into their simplest forms, called monosaccharides. The predominant one is glucose (sugar). Glucose is transported across the intestinal wall and into the bloodstream for delivery throughout the body- at this point it is termed your “blood (serum) sugar” and the measurement of this is your *serum glucose level*.

The human body strives to maintain the serum glucose level in a relatively narrow range- approximately between 70 mg/dl (milligrams per 100 milliliters of blood) and 100 mg/dl. The level may rise above 100 mg/dl after a meal, but the body takes steps to get the level back to the optimum range. It does so via mechanisms which include insulin- a hormone secreted by the pancreas, a long skinny gland found just behind the stomach. Insulin is secreted by specialized cells in the pancreas (beta cells) in response to a rise in the serum glucose level. Insulin fits into special receptors on the surface of various cells in the body, much like a key fitting into a lock. In the normal case, this then allows the glucose in the bloodstream to enter the cells. This provides the cells with the energy they need, and lowers the serum glucose level back to the desired range. As the serum glucose level goes down, the amount of insulin secreted by the pancreas goes down as well. Insulin has other effects as well, such as stimulating the production of fat, glycogen (storage carbohydrate) and protein in the body.

If the serum glucose level goes too low, the adrenal glands- two small triangular shaped organs which each lay just above the kidneys- release a different hormone known as a glucocorticoid hormone. This stimulates the conversion of glycogen, which has been stored primarily in the liver, to be broken down and converted into glucose. This glucose can then get into the bloodstream, thereby bringing the serum glucose level back up to the appropriate range.

What happens when serum glucose regulation is not optimal?

A large and rapid rise in serum glucose will cause the pancreas to respond quickly with a large quantity of insulin released into the bloodstream. Because this is a “panic” type of response, the quantity of insulin is typically more than that which would be needed to maintain serum glucose in the optimal range. This may lead to an overcorrection, with the serum glucose level then going lower than the optimal range. The adrenal glands respond with glucocorticoid hormone, leading glycogen stores in liver and muscle to be broken down, sending glucose back into the bloodstream. Since the adrenals were responding in an emergency type fashion, the glucose level may go too high, once more setting off an insulin response from the pancreas and starting the cycle anew.



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What contributes to wide serum glucose swings and high serum glucose levels?

A rapid and large rise in the serum glucose level can occur for a variety of reasons. Dietary factors play a large role. Millions of years ago our ancestors ate a high-plant diet with only minimal amounts of meat. The sugar from this type of diet is absorbed slowly and steadily. As hunting ability increased meat and fat played a larger role in the diet. The meat sources were more lean and lower in saturated fat than that seen today. Over the past 10,000 years agriculture became more developed, especially the cultivation of grains. In order to be consumed and digested, grains have to be crushed- a process that refines them and makes large amounts of carbohydrates available for digestion. Over the more recent half century there has been a rapid change in dietary habits. The foods which now dominate our diet are refined carbohydrates such as breads, pastas and cereals. Refined sugar, common in today's diet, is more highly concentrated, allowing for greater quantities to be consumed in a short time. Typically refined sugar may be ingested without fiber or other nutrients which could otherwise delay the absorption process. Diet is not the only factor but it appears to be a large one. As just one example, certain ethnic groups did not have serum glucose problems until they began eating foods high in refined sugars and carbohydrates.

What does this have to do with Weight Loss?

Wide fluctuations in serum glucose levels can make it extremely difficult to lose weight and keep it off- the patterns seen lead to a *weight loss resistant state*. In the face of a rapid and high rise in serum glucose, a burst of insulin is released from the pancreas. This insulin drives glucose into the cells. The priority storage areas are in the liver and muscle, where the glucose is converted into glycogen. Once these reserves are full, the glucose is converted into fat in our fat cells to be used as a longer term energy supply depot. Furthermore, it is felt that the liver and muscle cells become resistant to insulin more quickly and to a greater degree than fat cells. For a given level of insulin in the blood, the relative effect- promoting uptake of glucose- will be greater for the fat cells than for the liver and muscle cells. This leads to the fat cells taking in a higher amount of glucose more quickly and storing it as fat. As the body develops an increasing fat level, insulin resistance worsens and the cycle continues, making weight loss extremely difficult.

Animal research models have shown that when scientists inactivated the insulin receptors found in the brain, the animals showed increased food uptake and both males and females developed diet-sensitive obesity with increases in body fat. In a separate animal research model,



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researchers found that removing a component of the insulin receptor, thereby making the subjects insulin resistant, led to increased food intake and obesity. A third study showed that when the animals were kept insulin sensitive, even in the face of a high-fat diet they demonstrated significantly decreased body fat and resistance to weight gain.

The phase of the serum glucose swing where the blood sugar is below the optimal range is known as hypoglycemia. Typical symptoms include irritability, tremors, mood swings and-most importantly- tremendous food cravings, especially for sweets. This typically leads to excess food consumption and binge eating. The result is a rapid rise in serum glucose, starting the cycle over again.

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APPRESS™

APPRESS™ is not a prescription drug. It is an all natural, non-hormonal, non-synthetic proprietary blend of ingredients shown to have a positive impact on weight loss, serum glucose control, hunger level and energy level when used in conjunction with a diet low in refined carbohydrates (not calorie restricted) and an exercise program of 80 total minutes per week. **APPRESS™** supports weight loss by promoting glucose control, reducing hunger levels and promoting higher energy levels.

CLINICAL STUDY RESULTS

Reported effects are based upon a prospective, randomized, triple-blinded, placebo-controlled study conducted by an independent medical research center, with men and women with an average age of 43 who expressed an interest in taking the product for reasons primarily of weight loss.

There were no major differences between those randomized between placebo and treatment for the reason of not completing the trial. Both groups ate a diet low in refined carbohydrates but not calorie restricted. Both groups exercised three times a week for twenty minutes of light to moderate aerobic exercise, and two times a week for ten minutes of resistance training. There were no major adverse events that required IRB reporting. There was a *statistically significant reduction in body fat between the groups* at six weeks at a P value of 0.01. The average weight loss for those on product was 1.5 pounds per week. The subjects on **APPRESS™** lost almost *two times as much* as those on placebo. There was a *39.6% reduction in serum blood glucose level* one hour after a glucose challenge after six weeks of product compared to 12.3% for the placebo group, a statistical difference at a P value of 0.08. Significant glucose control was defined as greater than 50% improvement (reduction) in serum glucose level one hour following an oral glucose challenge after six weeks as compared to baseline. Of the group taking **APPRESS™**, *60% showed significant glucose control as compared to 14.3% of those taking placebo*. Complete glucose control was defined as greater than 85% improvement (reduction) in serum glucose level one hour following an oral glucose challenge after six weeks as compared to baseline. Of the group taking **APPRESS™**, 30% showed complete glucose control as compared to none of those taking placebo. Participants rated their subjective level of hunger through the study period. *70%* of those taking **APPRESS™** rated their average amount of hunger as improved *compared to 28.6%* of those taking placebo. Participants rated their highest amount of energy through the study period. 50%



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of those taking **APPRESS™** rated their highest amount of energy as improved, compared to 14.3% of those taking placebo

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Chromium

Chromium is a naturally occurring mineral essential to life. The trivalent form (Chromium III) is the most stable, both in nature and in biological systems. Trivalent chromium is available in the chloride or picolinate salt form. Trivalent chromium also occurs in organic complexes with nicotinic acid. Chromium is not produced by the body and must be obtained from the diet. The Institute of Medicine has determined that the RDI (Reference Daily Intake) for chromium is 120 mcg. The older RDA (Recommended Daily Allowance) for chromium set the range at 50-200 mcg. Unfortunately, the typical American diet, high in refined foods, supplies little chromium. Few foods are rich sources of chromium in the Western diet, the highest being organ meats, mushrooms, wheat germ and broccoli. The levels of chromium found in these foods may vary depending upon where they were grown or how they were processed. Furthermore, diets high in simple sugars compared to diets high in complex carbohydrates increase urinary chromium excretion in adults, possibly due to increased insulin secretion in response to the consumption of simple sugars¹. Research from the USDA found that American men ingest on average a mere 33 mcg of chromium per day, while American women only ingest an average of 25 mcg per day². Interestingly, even in diets designed by nutritionists to be well-balanced, the amount of chromium ingested is almost always less than 50 mcg³. The actual amount of chromium an individual needs varies, depending upon food intake and health status. In general, studies have shown that beneficial results from chromium supplementation were greater at higher levels compared to lower levels.

Chromium's function in our bodies is critical. It has long been known to be essential for proper carbohydrate and lipid metabolism in mammals⁴. Chromium takes part in the metabolism of glucose by enhancing the effects of insulin, secreted by the pancreas in response to increased blood glucose levels. Insulin binds to insulin receptors on cell surfaces, leading to an activation of the receptors which allows glucose to pass into the cell. The exact mechanism by which chromium helps in this process, and the precise structure of the biologically active form, is still not completely understood. Recent research proposes a model to help explain the role chromium plays. A low-molecular-weight chromium-binding substance (LMWCr), a naturally-occurring oligopeptide, has been shown to activate insulin receptor tyrosine kinase activity. The inactive form of the insulin receptor converts to the active form by the binding of insulin. This then stimulates the movement of chromium into the cell and leads to the binding of the chromium with the LMWCR. Once this takes place, the LMWCR binds to the insulin receptor and enhances its activity. Chromium levels are important because the ability of the LMWCr to activate or enhance the insulin receptor is dependent upon chromium levels⁵.

A report published in 1977 described a woman on long-term intravenous feedings which did not contain supplemental chromium. The patient developed severe diabetic symptoms which



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were vastly improved once chromium supplementation was undertaken⁶. Others noted similar findings, and chromium is now a standard part of long-term parenteral nutrition. It has also been recognized that infants who are malnourished and have impaired glucose tolerance respond well to oral supplementation with chromium⁷. Studies of male runners have shown that urinary chromium loss was higher during endurance exercise⁸, leading to the possibility that chromium needs may be greater in those participating in a regular exercise routine. Another study demonstrated that weight lifting was found to increase urinary excretion of chromium in men⁹.

There is an increasing body of data in the scientific community regarding the use of chromium supplementation to improve glucose tolerance in both diabetics and more recently in “pre-diabetics” or those at risk for developing type 2 diabetes. Kobla and Volpe reviewed current studies investigating chromium supplementation and found the majority to show improvement in glucose utilization or beneficial effects upon blood lipid profiles¹⁰. Ghosh et al conducted a double blind, placebo-controlled study examining chromium supplementation and its effects upon glycemic control and lipid profile in 50 subjects with type 2 diabetes. They found statistically significant improvement in glycemic control in the chromium group when compared to the placebo group¹¹. Anderson et al studied 180 people under treatment for type 2 diabetes. The groups were given daily doses of either 200 mcg of chromium, 1000 mcg of chromium, or placebo. Measurements at two and four months showed dramatic effects. Fasting and 2-hour insulin values decreased significantly in both groups receiving chromium as compared with placebo. Chromium also had significant beneficial effects upon Hemoglobin A1c, glucose, insulin, and cholesterol variables¹². In another publication, Anderson reviewed studies on chromium supplementation and noted that “chromium has been shown to play a role in glucose intolerance, Type 2 diabetes mellitus, and gestational diabetes”. He went on to comment that “the requirement for chromium is related to the degree of glucose intolerance: 200 mcg/day of supplemental chromium is adequate to improve glucose variables of those who are mildly glucose intolerant. However, people with more overt impairments in glucose tolerance and diabetes usually require more than 200 mcg/day”. He concluded “In summary, supplemental chromium has been shown to have beneficial effects without any documented side effects on people with varying degrees of glucose intolerance ranging from mild glucose intolerance to overt Type 2 diabetes mellitus”¹³. In a subsequent article on prevention of diabetes, Anderson writes that “Suboptimal dietary intake of chromium is associated with increased risk factors associated with diabetes and cardiovascular diseases. Within the past five years, chromium has been shown to improve glucose and related variables in subjects with glucose intolerance and type 1, type 2, gestational and steroid-induced diabetes”¹⁴.

Chromium has shown beneficial effects not only in diabetics but in those with glucose intolerance or pre-diabetes. Bahijri measured the effects of chromium supplementation on 44 non-diabetic adults in a double blind placebo-controlled cross-over study. Those taking the chromium demonstrated a statistically significant improvement in both lipid profile and in serum glucose control¹⁵. Lamson and Plaza reviewed the safety and efficacy of chromium and found “the beneficial effects of chromium on serum glucose and lipids and insulin resistance occur



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even in the healthy”¹⁶. Preuss et al noted that “ingestion of niacin-bound chromium and natural antioxidants...has been demonstrated to improve insulin sensitivity and/or ameliorate free radical formation and reduce the signs and symptoms of chronic age-related disorders including syndrome X”¹⁷. In a double blind, placebo-controlled clinical trial, Cefalu et al followed 29 participants who were overweight and at risk for developing Type 2 diabetes. One group received 1,000 mcg of chromium, the other group received placebo. Those on the chromium demonstrated significant improvement in insulin sensitivity at both four and eight months, demonstrating that chromium supplementation can improve insulin sensitivity in individuals who are overweight and pre-diabetic¹⁸.

Kaats et al performed a randomized, double blind placebo-controlled study of 154 subjects receiving 200 mcg or 400 mcg or placebo for 72 days. Both groups taking the chromium showed significant gains in lean body mass and decreases in body fat compared to those receiving placebo¹⁹. In a subsequent study, Kaats et al performed a double blind, placebo-controlled study on 122 moderately overweight individuals. One group took 400 mcg of chromium daily, the other took placebo. Those taking chromium demonstrated a statistically significant reduction in body fat (without loss of lean body mass) compared to those taking placebo²⁰.

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Banaba Leaf (*Lagerstroemia speciosa*)

Banaba is a medicinal plant found in the Philippines, India and various parts of Southeast Asia. Banaba has a long history of use as a folk medicine among diabetics in the Philippines. It contains colosolic acid, a triterpene compound also known as 2-alpha-hydroxyursolic acid. The first laboratory research study published on colosolic acid was by Murakami et al from the Hiroshima University School of Medicine, Japan in 1993. They found that colosolic acid acted as a glucose transport activator¹. Kakuda et al then conducted a study using extracts of *Lagerstroemia speciosa* leaves in mice with hereditary diabetes (Type II, KK-AY/Ta Jcl). When the mice were fed cellulose, plasma glucose rose accordingly. This rise in serum glucose was almost entirely suppressed by giving the mice the extract. Plasma total cholesterol level, serum insulin and amount of urinary excreted glucose were all lower in the mice fed the *Lagerstroemia speciosa* extract². Suzuki et al then performed a study using the same strain of mice and extracts from *Lagerstroemia speciosa*, looking at the effect of the extract on weight. Animals were fed either a control diet or a diet that also contained the extract. Neither group demonstrated a change in total diet intake during the study period of 12 weeks. The group ingesting the extract demonstrated a significantly lower weight gain compared to the control group³.

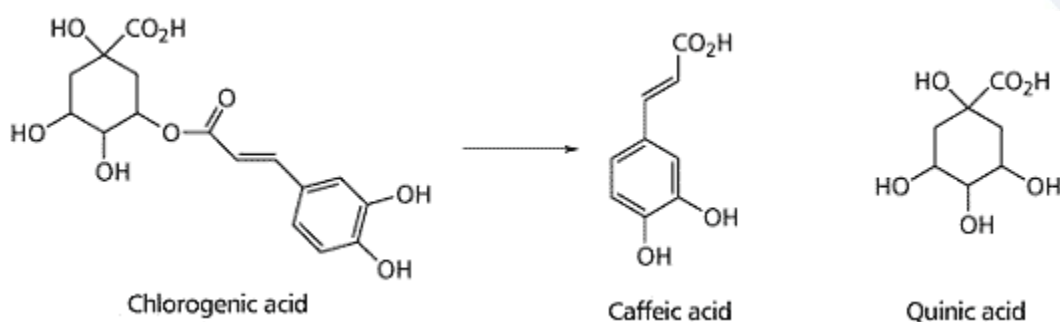
Liu et al examined the effects of extracts from *Lagerstroemia speciosa* L. on glucose transport and adipocyte differentiation utilizing a radioactive assay. Those cells exposed to the extract showed a statistically significant increase in glucose uptake and decrease in adipocyte differentiation, leading the authors to conclude that the extract “may be useful for prevention and treatment of hyperglycemia and obesity in Type 2 diabetics”⁴. Building upon this research, Hayashi et al looked for specific compounds in the extracts which may be responsible for the glucose transport activity. They performed bioassay-guided fractionation of the aqueous acetone extract of the *Lagerstroemia speciosa* leaves. They identified three active ellagitannins- lagerstroemin, flosin B and reginin A, which increased glucose uptake of rat adipocytes⁵. Hattori et al then examined one of the ellagitannins- lagerstroemin- and its effects upon rat adipocytes. They found the compound increased the rate of glucose uptake and decreased glycerol release, noting that lagerstroemin had definite insulin-like actions⁶.

Judy et al used a standardized extract from *Lagerstroemia speciosa* leaves in a randomized trial on human subjects with Type 2 diabetes. Subjects received either 32 mg or 48 mg of the standardized extract daily. There was a 30% decrease in blood glucose levels in those taking the extract in a gelatin form as opposed to a 20% drop in those on the dry-powder formulation⁷.

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Gahwa bean extract- Chlorogenic Acid



Chlorogenic acid and its ester, caffeic acid, are natural polyphenols found in certain herbs and in green coffee beans. These polyphenols have significant health-promoting attributes. They have known potent antioxidant properties, and more recently they have been shown to have an impact upon carbohydrate metabolism. They play a role in the reduction of lipid peroxidation, imparting significant potential cardiovascular benefits.

Chlorogenic acid has been the subject of laboratory investigation due to its role in assisting the body in regulation of serum glucose. In the liver, the multi-component glucose 6-phosphatase (Glc-6-Pase) system plays a key role in the regulation of serum glucose. This system is involved in the final enzymatic step of gluconeogenesis and glycogenolysis, both of which serve to increase serum glucose levels. In 1997, Arion et al published an article noting chlorogenic acid as a newly found inhibitor of hepatic glucose 6-phosphatase¹. Hemmerle et al shortly afterward studied chlorogenic acid and various derivatives in microsomes of rat liver, showing a dose-dependent inhibition of gluconeogenesis and glycogenolysis. They concluded that these inhibitors “may be useful for the reduction of inappropriately high rates of hepatic glucose output often found in non-insulin-dependent diabetes”². Herling et al showed that a derivative of chlorogenic acid produced concentration-dependent inhibition of gluconeogenesis and glycogenolysis, and also prevented the hyperglycemic peak typically seen after glucagon exposure³.

In an in vivo study, Rodriguez de Sotillo and Hadley examined the effects of chlorogenic acid upon obese, hyperlipidemic, insulin resistant (fa/fa) Zucker rats. Chlorogenic acid



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significantly lowered the postprandial peak response to a glucose challenge compared to the same group prior to receiving the chlorogenic acid. Furthermore, in the chlorogenic treated rats, fasting plasma cholesterol and triacylglycerol concentrations showed significant decreases of 44% and 58% respectively. Chlorogenic acid demonstrated an invivo ability to improve glucose tolerance⁴. A human clinical evaluation of chlorogenic acid was performed in Moscow. Abidoff studied 75 healthy volunteers, with each receiving either 90 mg of chlorogenic acid or placebo prior to a test meal. Results showed that the chlorogenic acid group had lowered the increase in blood glucose level by 15-20 percent⁵. It is known that coffee is one of the primary sources of chlorogenic acid in the human diet. In an intriguing cohort study that evaluated coffee consumption and the risk of type 2 diabetes mellitus, van Dam and Feskens found that even after adjustments were made for potential confounders, higher coffee consumption was associated with a substantially lower risk of clinical type 2 diabetes⁶.

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Gurmar (Gymnema sylvestre)

Gurmar is a hindi name meaning “destroyer of sweet”. When the leaves of this woody, climbing plant are chewed, the tongue becomes insensitive to the taste of sweetness for about an hour. The Latin name for this plant is *Gymnema sylvestre*, native to the tropical forests of central and southern India. It was felt by Ayurvedic doctors that if the plant neutralized the taste of sweetness on the tongue, it may have effects upon sugar levels in the body. Indeed, it has been used for generations in India for those with diabetes.

Gurmar contains a number of constituents, including saponins, resins, quercitol, stigmasterol, and triterpene glycosides¹⁻³. Gurmar has different effects and influences upon glucose metabolism and serum glucose levels. Two studies on diabetic rats found that gurmar extracts increased the number of insulin-secreting beta cells in the pancreas and helped bring blood sugars close to the normal level^{4,5}. In other animal models Gurmar was found to stimulate insulin release^{6,7}, inhibit peripheral utilization of glucose⁸, and increase the activity of enzymes which are responsible for the uptake and utilization of glucose⁹.

Studies have been done in humans exploring the effects of Gurmar upon blood glucose levels, especially in those with diabetes. A controlled study done in 1990 followed subjects with type 1 diabetes given a standardized Gurmar extract. While the control group showed no significant reduction in blood sugar levels or insulin requirements, those in the group receiving Gurmar dropped their average blood glucose from 232 to 152 mg/dL. There was also a statistically significant decrease in glycosolated hemoglobin (HbA1c) after 6 months compared to the control group¹⁰. Another human study examined the effect of an extract of Gurmar upon subjects with type 2 diabetes also taking conventional oral anti-hyperglycemic agents. Subjects took the extract for 18 to 20 months, and during this time they had a significant reduction in blood glucose levels, glycosolated hemoglobin and glycosolated plasma protein levels. Subjects were able to decrease the dosage of their conventional drugs, and 5 of 22 diabetic patients were able to discontinue their conventional drugs and use only extract alone¹¹.

A review from a group at Harvard Medical School looked at the published literature on the efficacy and safety of herbal therapies and vitamin/mineral supplements for glucose control in patients with diabetes and found Gurmar to be among the supplements with positive preliminary results¹². A group from Georgetown found that the combination of Hydroxycitric acid, Chromium and Gurmar extract facilitated a reduction in body weight and body mass index while at the same time promoting healthy blood lipid levels¹³.

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Cynara scolymus

Cynara scolymus is a member of the milk thistle family. It is one of the world's oldest medicinal plants and has been used by the ancient Egyptians, Greeks and Romans. The plant contains a number of active constituents, including cynarin, caffeic acid, chlorogenic acid, flavonoids and other polyphenolic compounds^{1,2}. Studies have demonstrated that components of Cynara scolymus have marked protective properties against oxidative stress induced by inflammatory mediators in vitro³. These in vitro properties were shown to hold as well in an in vivo rat model, where the protective activity of Cynara scolymus was again demonstrated⁴. A human study of cynarin involved 2 groups of 30 patients with blood lipid abnormalities. The group taking cynarin had a significant reduction not only in cholesterol and pre-beta-lipoprotein levels, but in body weight as well⁵.

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Vanadyl sulfate

Vanadium is a naturally occurring metallic element which has recently been identified as being essential in the human diet. The common form found in supplements is Vanadyl sulfate. While no Recommended Dietary Allowance has been established, a typical diet provides 10 to 30 micrograms of vanadium per day. Foods containing vanadium include parsley, mushrooms, shellfish and wine. Vanadium appears to play a role in carbohydrate metabolism as well as in the metabolism of cholesterol and other lipids.

Vanadyl sulfate appears to have insulin-like effects. This has been shown in animal and human models. In studies done on animals, Kordowiak et al found insulin-like effects on liver Golgi membrane preparations¹, while Mosseri et al showed that Vanadyl inhibited hepatic glucose-6-phosphatase and phosphoenolpyruvate carboxykinase, playing “an important role in reducing blood glucose levels”². Shinde et al, using a form of Vanadyl, found it to improve glucose and lipid homeostasis “due to the insulin sensitizing action of vanadium”³.

In human trials, a placebo controlled study showed that 3 weeks of Vanadyl sulfate improved hepatic and peripheral insulin sensitivity in patients with non-insulin dependent diabetes⁴. Boden et al performed a blinded, placebo-controlled study which demonstrated that vanadyl sulfate was well tolerated and resulted in reductions of fasting plasma glucose and hepatic insulin resistance⁵. Goldfine et al found that when given to patients with insulin-dependent-diabetes, Vanadate led to a statistically significant decrease in insulin requirements⁶.

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Pterocarpus marsupium

Pterocarpus marsupium is a deciduous tree with a long history of use in Ayurvedic medicine. Numerous studies have been done using concentrated extracts of the bark and heartwood of the tree. Constituents of Pterocarpus marsupium include (-)Epicatechin, marsupin, pterosupin, pterostilbene, and a variety of flavonoids (Ref 1). The role of Pterocarpus marsupium and other Indian plants in the management of serum glucose has been recently reviewed (ref 2, 3).

(-)Epicatechin is an active component and has been found to have insulinogenic and insulin-like properties in animal models (ref 4). (-)Epicatechin has been shown to have antidiabetic effects and help promote pancreatic beta-cell regeneration in rats (Ref 5,6). A study of three components of Pterocarpus marsupium (masupsin, pterosupin and pterostilbene) in hyperglycemic rats demonstrated a significant reduction in blood glucose levels, with an effect comparable to the drug Metformin (ref 7). Grover et al showed that an extract of Pterocarpus marsupium corrected the alteration in phosphofructokinase, a key enzyme of carbohydrate metabolism, in an animal model (Ref 8). Kar et al confirmed the blood glucose lowering effect of 30 different Ayurvedic medicinal plants, with Pterocarpus marsupium having the 4th highest activity (ref 9). A flexible dose open trial among humans was performed in 4 centers in India using Pterocarpus marsupium. In looking at the 93 patients who completed 12 weeks of taking the supplement, there was a statistically significant reduction in both the fasting and postprandial blood glucose level. There was also a statistically significant decrease in mean HbA1c as well (Ref 10).

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Galega officinalis

Galega officinalis, also known as Goat's rue or French lilac, has been used for blood sugar problems since medieval times, when it was prescribed to relieve the intense urination associated with what came to be called diabetes. The main constituent thought responsible for its effect on lowering blood sugar is galegine (isoamylenguanidine), and research on this compound has been going on for over half a century¹. Guanidine-based prescription medications came into use in the 1950's. Phenformin and buformin had unacceptable side effect profiles, but Metformin, a biguanide, is safer and is widely used today². Galega officinalis also contains flavonoids and sponins.

More recent investigations have looked at the hypoglycemic and the antidiabetic activity of Galega officinalis^{3,4}. Galega officinalis has been used in conjunction with other plant extracts in a laboratory setting with marked hypoglycemic effects⁵. Palit et al reported their findings that in an animal model, in addition to the serum glucose lowering effects, "Galega has a novel weight reducing action that is largely independent of a reduction in food intake"⁶.

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Biotin

Biotin is a member of the B-vitamin family and is an essential nutrient for humans. It is a bicyclic compound with eight stereoisomers, only one of which is found naturally. Biotin is involved in the biosynthesis of fatty acids, metabolism of branched-chain amino acids, and in gluconeogenesis. It is a critical component of several enzymes involved in energy metabolism as well.

Biotin has been studied for its role in a variety of conditions, including its effects on lipid metabolism and glucose stabilization (Ref 1). Furukawa studied the effects of biotin on glucose-induced insulin secretion in an animal model and found evidence for a direct effect upon the pancreatic beta cells. He concluded “these results indicate that the administration of high concentrations of biotin may improve the metabolism and/or utilization of glucose in patients with non-insulin-dependent diabetes mellitus” (Ref 2). Romero-Navarro et al, using an animal model, found that “biotin affects pancreatic islet glucokinase activity and expression and insulin secretion in cultured islets” (Ref 3). McCarty has written about the uses of Biotin in conjunction with chromium to assist in glycemic control (Ref 4).

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