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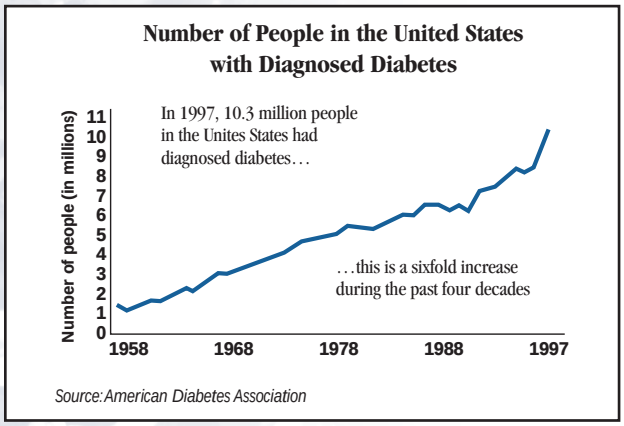
DIABETES – THE PREVENTABLE EPIDEMIC

Diabetes is the 7th leading cause of death among Americans and cases of this disease are growing at an alarming rate. Without exaggeration diabetes is becoming a modern, albeit silent, epidemic. Currently, over 10 million Americans are diagnosed with some form of diabetes, while another 5 million are considered to be diabetic without their knowledge. What makes this information so tragic is the fact that most of these individuals may have been able to prevent the onset of the disease with proper awareness, diet and exercise. The modern Western diet and lifestyle has done much to lead our generation to the threshold of insulin resistance, and with it, the collection of symptoms known as Syndrome X. This issue will review some of the basics of preventable diabetes (type II) and the consequences of poor glycemic control leading to insulin resistance. The major focus will be on the accumulated research of various nutraceuticals as they have been used to treat or prevent diabetes and its harmful complications.

Diabetes mellitus is a metabolic disorder characterized by elevation of fasting blood sugar (glucose). While the cause of the elevated blood glucose may be associated with either too little or too much insulin, the complications of chronically high serum glucose is devastating to the individual. Complications of uncontrolled blood sugar include increased risk of heart disease, stroke, kidney disease, blindness, and loss of nerve function. Regulating blood sugar for diabetics is therefore crucial to both the immediate as well as long-term care of diabetic patients.



Type I diabetes

Often called insulin dependent diabetes mellitus (IDDM), this form of diabetes is characterized by the destruction of the pancreatic beta cells that manufacture insulin. Typically this form is diagnosed while the patient is a child or adolescent and requires insulin for the management of blood sugar. Many theories have attempted to account for the damage of these important insulin-producing cells including autoimmune processes, chemical damages, viral infection, and genetic disposition. Whatever the cause, the result is very low or no insulin; a protein that is the primary mediator of glucose transport into cells. This diminished insulin level leads to elevated levels of glucose in the blood, which then results in numerous complications. Of the more than 15 million Americans with diabetes, only about 10% are considered to have type I diabetes.

Type II diabetes

Almost 90% of diabetics are considered to have non-insulin dependent diabetes mellitus (NIDDM) or type 2 diabetes. While also characterized by high blood glucose levels, type II diabetics often have high, rather than low,

In My Opinion

Being a research scientist, as opposed to a clinician, there is one particular aspect of treating diabetes with which I am amazed. If you will permit me to speak as a clinical outsider– it seems to me that type 2 diabetes, as an epidemic, can be and should be stoppable. Unfortunately, as you and I know, it will likely go on– relatively unabated. How is it that what is essentially a preventable disease, with devastating consequences, is marching on with no end in sight?

As this is ostensibly a Western disease, our answer lies in understanding the Western view of the world; and the sacredness placed on lifestyle. You have probably all experienced the pained look of a patient who is told that their diet and lifestyle must be changed in order to alter their health. They wonder, is it really a must? Or is there some alternative that can be found? Some drug, some supplement? As we have outlined within this review, there are many natural ingredients that can help, but in the absence of lifestyle changes (diet, exercise, stress management etc) these are only delaying the inevitable. We need something to overcome the Western paradigm that first asks "**Why** must I do it?" before asking "**What** must I do?". If we don't have an answer, they won't have a prayer.

The answer, I am convinced, lies in how persuaded you, as the clinician, are about these things– to the extent that you actually practice them in your own lifestyles and homes. A supplement or a prescription is one thing, but to get them to turn their whole world upside down requires some real convincing. The role of educator, in this case, is more than an academic exercise– it is teaching by example. I believe that if all of those dispensing health advise across this country were to live the recommendation they give to their patients or clients, we would see an overnight turn-around in this epidemic. At least we could give the food-advertising juggernaut a run for their money.

Those clinicians, to whom I speak, who have taken their own recommendations to heart for their own life seem to have more confidence in convincing patients of needed changes. They have an enthusiasm for dietary changes that is tangible, and their patients are excited about the possibilities rather than fear the unknown. When they are asked for a recipe, they have many to share– as well as personal tips on which are the best. By the time they are finished– the patient will forget about "**Why** must I do it?" and immediately ask "**What** must I do?" This, I believe, is the first step in ending the epidemic. I should know, I've been checking my own cupboards all week….

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levels of serum insulin. Type 2 diabetics are typically insulin resistant, rather than insulin depleted. A current report in JAMA concludes that nearly one-fifth, or 47 million Americans are at an increased risk of type 2 diabetes, using the criteria of abdominal obesity, elevated triglycerides, low HDL cholesterol, high blood pressure and high normal blood sugar (1). In this report, these symptoms were called "metabolic syndrome", but many people already know them as "Syndrome X". This syndrome and the subsequent diabetic condition that follows are preventable. Through an awareness of the various risk factors, proper diet and exercise; type 2 diabetes could be altered from a national epidemic to a manageable but minor disease. History tells us, unfortunately, that the Western diet and lifestyle have a tenacious hold on the American culture and this trend toward obesity, insulin resistance and diabetes is unlikely to abate anytime soon.

Diabetic Complications

Hyperglycemia (high blood glucose) causes complications in patients with diabetes, regardless of whether it is type 1 or 2. While some complications can be of an acute nature (ketoacidosis due to low insulin or hypoglycemic shock due to insulin overdose), most complications are a result of years of unregulated and high serum glucose. These complications include increased heart disease, retinopathy, nephropathy ending in renal failure, neuropathy, foot and leg ulcers, impotence, and the inhibition of many important metabolic enzymes. Most of these complications are due to hyperglycemic-induced increase reactive oxygen species (ROS) that cause glucose-induced activation of protein kinase C, increased formation of glucose-derived advanced glycation end products (AGEs) and increased glucose flux through the aldose reductase pathway (2). These vascular complications are cumulative, but preventable. Maintaining proper blood glucose is vital to preventing these complications. Additionally, there are a number of natural ingredients that can prevent and even reverse the progress toward these devastating complications.

Syndrome X and Insulin Resistance

Syndrome X is the name given to a collection of metabolic conditions; highlighted by insulin resistance, but also includes obesity (especially in the abdomen), high cholesterol, low HDL cholesterol, high triglycerides and hypertension. These symptoms are often termed pre-diabetic syndrome. Insulin resistance is one of the key features and dangers of this syndrome. Insulin resistance is a condition where the pancreas is able to manufacture more than enough insulin, but cells have become resistant to insulin's effects. This increases blood glucose as well as stimulates insulin-induced metabolic functions (conversion of carbohydrates to fats leading to obesity). The constant intake of refined carbohydrates, leading to dramatic spikes in blood glucose followed by dramatic spikes in insulin secretion, is the primary cause of insulin resistance and then

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type 2 diabetes. It is for this reason that diet is possibly the most important aspect to the treatment and prevention of type 2 diabetes and its precursor condition, Syndrome X.

Diet and Lifestyle are vital

It is difficult to over emphasize the importance of diet as it pertains to preventing and treating type 2 diabetes (many of the principles discussed here are applicable to type 1 diabetes as well, the role of therapeutic levels of insulin in these patients has nuances that are not discussed here). Since diabetes is a metabolic disorder, food can be considered either a poison or a therapy depending on its content. Not only can food lead to obesity, food is the primary foundation for blood sugar control– often called glycemic control or balance. The steady balance or glycemic control is the key to prevent and treat syndrome X and type 2 diabetes. Avoiding foods that destabilize glycemic balance and eating foods that promote glycemic balance is the key to a healthy diet for everyone, but especially for those with insulin resistance.

Since this review is primarily focused on therapeutic natural ingredients, so-called nutraceuticals, this will only provide basic principles for the diet. More information should be gathered from a resource designed specifically with that subject in mind, some of which are provided in the general reference section at the end of this review.

General Guidelines

- Understand that glycemic index and total carbohydrates may differ dramatically
- Avoid most processed foods regardless of their protein:carb ratio
- Avoid trans-fatty acids and increase omega-3 fatty acids and GLA
- Increase dietary fiber
- Avoid or test for commonly allergenic foods (dairy, gluten etc)
- Avoid refined sugar in all its forms
- Avoid alcohol
- Avoid artificial sweeteners like aspartame– try stevia or xylitol instead
- Drink plenty of pure water
- Don't assume anything– Read the label.

Other lifestyle factors are also important for those with diabetes or syndrome X. Among them, exercise and stress management are vital. Physical activity and regular exercise may not only have direct impacts on glucose use and insulin sensitivity, but also on many risk factors such as obesity, triglycerides, and hypertension. In a recent study, exercise had significant improvement on the vascular function in type 2 diabetics (62). It should be noted that patients taking pharmaceuticals to reduce blood sugar or insulin should be monitored during exercise to prevent hypoglycemia. Typically, less hypoglycemic medication is required during physical activity. If the patient is not physically active, a slow progression into an exercise program with consistent monitoring of blood sugar is prudent. In a study just published in New England Journal of Medicine, effective lifestyle changes were compared to a popular oral hypoglycemic in preventing type 2 diabetes in patients with pre-diabetic hyperglycemia (69). In this study, 3234 "pre-diabetic" patients were given either metformin (Glucophage®- 850 mg b.i.d.), put on a lifestyle modification program (goals of 7% reduction in weight and 150 minutes of physical activity per week), or placebo. Each group was instructed with the same dietary guidelines. After almost 3 years, there were 31% fewer diabetics in the drug group versus placebo, but there were 58% fewer diabetics in the lifestyle group than placebo. Lifestyle modification was significantly more effective than metformin in this study, not to mention the other benefits gained by weight reduction and increased physical activity.

Another key factor is stress management. Along with the pancreatic production of insulin, the adrenal glands are important in the regulation of blood sugar. The adrenal hormone cortisol is stimulated whenever the body is "under stress". Whether this stress comes from mental or emotional stress, chronic inflammation, food allergies, or low blood sugar; cortisol effectively raises blood glucose levels by stimulating gluconeogenesis. This raised glucose level can exceed desired levels when stress-induced cortisol levels are extremely high (alarm reaction). Chronic glycemic imbalance or other stress could then result in both reduced insulin sensitivity and adrenal exhaustion. Studies have shown that glycemic control of diabetics with higher measurable stress is worse than those with lower measurable stress and, additionally, techniques to reduce stress lead to better glycemic control among diabetic patients (3,4,5). Reports have also directly linked the function of the hypothalamic-pituitary-adrenal axis with the risk of type 2 diabetes (11). An excellent way to determine adrenal stress is by measuring salivary cortisol throughout a single day (See The Standard vol. 3 no.1 for a complete discussion of diagnosing and treating adrenal stress).

Natural Treatments

The first goal in therapy is to reach and maintain an optimal fasting blood glucose level. This can be done in a way that benefits other metabolic outcomes such as improving lipid profiles and reducing blood pressure. The second goal in therapy is to prevent and treat the chronic consequences and complications associated with years of poor blood sugar control.

Supplemental Fiber

Dietary fiber is an important aspect of blood sugar control. The addition of water-soluble fibers such as gums, pectins, and mucilage are capable of reducing the speed at

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which carbohydrates are absorbed and increase tissue sensitivity to insulin. This has been of benefit for both type 1 and type 2 diabetics (6,7). The use of psyllium husk powder (5 grams twice daily 20-30 min. before meals) has been shown to reduce fasting and postprandial blood glucose levels as well as improve lipid profiles in type 2 diabetics, when compared to placebo in double-blinded studies (8). Other studies had similar results when giving type 2 diabetics 5 grams of psyllium before each of three meals daily (9). Long-term favorable effects on glycemic control and lipid concentrations are also associated with 15g/day of supplemental guar gum (10). Adding supplemental fiber to the diet, in the form of a psyllium or similar product can be an excellent way to keep and maintain glycemic control. Increase in soluble dietary fiber will promote healthy bowel transit times and benefit the gut microflora as well.

Essential Fatty Acids

The role of essential fatty acids is critical in the overall health of diabetics as it is with all individuals. For a complete review of essential fatty acids and their role in diabetic therapies see The Standard Vol. 3 no. 2. In summary, the decreased conversion of the essential omega-6 fatty acid linoleic acid into gamma-linolenic acid (GLA) in diabetic patients leads to the therapeutic benefit of ingesting GLA-rich oils such as borage and evening primrose. The greatest benefits of GLA supplementation are increasing nerve conduction and the improvement of skin related disorders. Additionally, omega-3 fatty acids from flax seed oil or fish oil supplementation should be considered as well. The benefit of these oils in diabetic patients is primarily in their relationship to the cardiovascular system, an area which diabetics are vulnerable due to increased lipid peroxidation, atherosclerosis, cholesterol and other lipid disorders. The long chain EPA and DHA found in fish oils are also necessary for the retina in particular, a tissue that is often damaged after years of poor blood sugar management (diabetic retinopathy– See The Standard Vol. 2 no. 1 for more information about treating diabetic retinopathy). The reduction of oxidized and trans-fatty acids and the increase of high quality essential fatty acids should be a goal for everyone, but especially for those who have, or are susceptible, to type 2 diabetes.

Micronutrients and Nutraceuticals

While the role of diet and lifestyle is fundamental to improving outcomes for diabetic patients, supplemental nutrients and natural therapeutic ingredients can also play a vital role in patient care. Tissue levels of B-vitamins are significantly depleted in animal models of diabetes (19) as has also been reported in humans with diabetes. A high quality multivitamin-mineral product should be the basis of supplemental therapy, one with adequate levels of B-vitamins, vitamin C and magnesium. Below are additional micronutrients and nutraceuticals that should be considered in the treatment of diabetic and syndrome X patients.

Chromium

Chromium is a key constituent in the molecule known as glucose tolerance factor (GTF). This complex facilitates the uptake of glucose into cells in conjunction with insulin, somewhat like a cofactor to insulin. A recent study compared the supplemental intake of 200 mcg of Cr/day, 1000 mcg/day Cr or placebo on the glucose and insulin variables of 180 men and women with type 2 diabetes. While they noted some improvement in the 200 mcg/day group, the group taking 1000 mcg/day had statistical improvements in HbA_{1c} (glycosylated hemoglobin), fasting glucose, insulin and cholesterol levels when compared to placebo (12). Additionally, research has concluded that non-insulin dependent diabetic patients have a compromised chromium status, when compared to healthy controls. The researchers speculate that this is one of the factors leading to insulin resistance in these patients (13).

Vanadium

For some time, vanadium has demonstrated an insulin-like property in isolated cells and tissues and has been considered to have therapeutic potential for diabetic patients. What has been described as an insulin-mimetic activity by most researchers may actually be an insulin-enhancing function (14). Regardless of the mechanism, vanadium has been used clinically to help manage serum glucose levels. A small study showed that 100 mg/day of vanadyl sulfate (VS) for three weeks was able to significantly improve hepatic and peripheral insulin sensitivity in insulin-resistant NIDDM patients. These effects were even sustained for as much as 2 weeks after discontinuation of vanadyl sulfate (15). This same dose did not alter insulin sensitivity in non-diabetic individuals, suggesting a corrective role for vanadium (16). The safety and efficacy of 100 mg/day of VS has been tested and shown to be quite good (17), and other studies have been successful and safe at even higher doses (18). It should be noted that chronic use of vanadium at these high doses has not been validated; and a lower dose may be helpful when used in combination with other natural remedies.

Biotin

The importance of this vital micronutrient produced by healthy gut microbes has often been overlooked in the management of diabetics. Biotin has a number of relevant activities including stimulation of glucose-induced insulin secretion, enhancing insulin sensitivity, and the acceleration of glycolysis in the liver and pancreas by its enhancement of the enzyme, glucokinase (24). Biotin supplementation has been shown in both insulin-dependent and non-insulin dependent diabetic animal models to improve glucose and insulin tolerances (20,21). In humans, improvements in

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oral glucose tolerance tests as well as diabetic related neuropathy symptoms are associated with increased biotin intake (22, 23).

Alpha Lipoic Acid

Also known as thioctic acid, alpha lipoic acid is a natural and versatile antioxidant with numerous therapeutic uses. As an antioxidant it is able to "recharge" vitamin C, vitamin E and glutathione because of its three-fold water-soluble, fat-soluble and sulfhydryl properties. In the case of impaired glucose metabolism and the complications associated with diabetes, the actions of lipoic acid are quite helpful. Not only does lipoic acid modulate glucose and insulin sensitivities but acts as to prevent and treat many of the oxidative damages that occur with hyperglycemia. One recent study compared insulin sensitivity in type 2 diabetics after one month of placebo, 600 mg/day, 1200 mg/day, or 1800 mg/day oral lipoic acid (25). They found that the treatment, regardless of dose, was equally able to improve insulin sensitivity by 27% over placebo. This data confirmed research they had done previously by intravenous administration (26,27).

As an antioxidant, lipoic acid is capable of decreasing oxidative stress, the main stimulus for diabetic complications. A cross-sectional study was performed to assess the oxidative load (by looking at lipid peroxide levels) in diabetic patients some of which were taking 600 mg lipoic acid per day for 3 months (28). The lipoic acid group had 36% lower levels of lipid peroxides and a 38% improvement in the ratio between oxidative stress and oxidative defense (measuring lipid peroxides vs. alpha-tocopherol/cholesterol levels). These data confirm the antioxidant role of lipoic acid in these patients with poor glycemic control, a group prone to oxidative stress and damage.

Perhaps the longest use of lipoic acid in diabetes is in the treatment of diabetic neuropathy. Lipoic acid has been used in Germany for over 30 years for the treatment of diabetic-induced neuropathy (29,30). Its mechanism of action seems to be related to its antioxidant activity leading to improved microcirculation and a positive influence on impaired neurovascular reflex arc in patients with diabetic neuropathy (34,35). While most of these studies were performed using intravenous delivery, recent studies confirm that similar results can be obtained by oral administration of 800 mg/day (31) or in other studies 600 mg t.i.d. (32). However, one study showed only marginal favorable effects when using 600 mg t.i.d. in a multicenter controlled trial (33). Clearly more data must be gathered in the use of lipoic acid in long-term studies, but it is clear from the available literature that the use of lipoic acid is a vital and safe component to nutraceutical therapy in diabetic patients, as well as those with metabolic insulin disorders like syndrome X. The use of high oral doses of lipoic acid should be accompanied with biotin to prevent competitive inhibition of biotin-dependent enzymatic processes (36).

There are many other nutraceuticals that have been used successfully in the treatment of diabetic patients. Those that have a positive effect on lipid or carbohydrate metabolism, increase general metabolism or weight-loss, or inhibit the formation of sorbitol may be beneficial for preventing or treating diabetes. These may include carnitine, niacin, zinc, quercetin (or similar flavonoids) and lipotropic agents like inositol and choline to name only a few. These and others are likely to be the focus of attention in *in vitro*, animal, and clinical research in the near future.

Herbs and Botanical Extracts

The use of various plants and their extracts for diabetes (sugar in the urine) has been common since ancient times. Recently, we have been able to scientifically investigate the use of several botanical extracts for their hypoglycemic and insulin modifying effects. This review will discuss those with the most research and potential for therapeutic use as nutraceuticals in the U.S.

Gymnema sylvestre

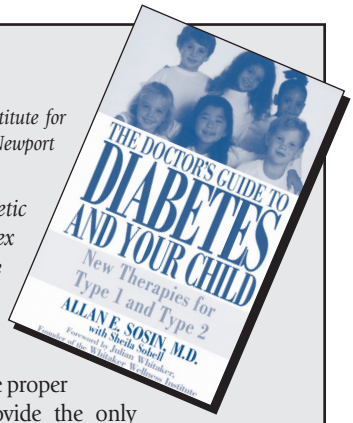
Gymnema is a woody plant that grows in the central and southern parts of India, where it has been used for almost two millennia for the treatment of diabetes. Some preliminary research was conducted on this plant over 70 years ago but most of what we know of its hypoglycemic properties has been learned in the past 20 years. The activity is thought to reside primarily in a group of compounds called gymnemic acids, of which extracts are usually standardized. In animal studies, gymnema leaf powder was able to control blood sugar levels as well as other insulin-dependent metabolic pathways (37,38).

One particular extract, known as GS4, has been used in clinical trials with both insulin-dependent and non-insulin dependent diabetic patients. In IDDM patients given 400 mg/day GS4, insulin requirements were reduced as well as fasting blood glucose levels, perhaps by increasing insulin usage or residual beta cell function (39). This same gymnema extract was able to double the number of pancreatic beta cells when given to diabetic rats (40). Likewise, this research group also investigated the use of 400 mg/day GS4 in 22 Type 2 diabetic patients who were taking conventional oral anti-hyperglycemic medications. After 18-20 months of Gymnema extract use, the patients showed a significant reduction in blood glucose, glycosylated hemoglobin and reduction in conventional drug use. Five of the 22 discontinued medication altogether and insulin levels in these patients were increased after taking GS4 (41).

Several mechanisms are thought to account for the hypoglycemic activity of gymnema extracts. As mentioned previously, gymnema extracts are associated with increased pancreatic function and insulin release. While recent studies have confirmed these results in animals (42), *in vitro* tests

Clinical Approaches

With Allan E. Sosin, M.D., Author of The Doctor's Guide to Diabetes and your Child. Dr. Sosin is the Director of The Institute for Progressive Meidicine in Irvine, California. He was previously the Medical Director of the Whitaker Wellness Institute in Newport Beach.



Question: *What is the most common mistake that you believe is made in treating diabetic patients?*

Answer: Starting them on medication without first making lifestyle changes. If the medication is initially effective in controlling the blood sugar, the patient may not implement essential lifestyle changes to prevent future problems. Elevated blood sugar is only a single factor in a combination of problems that have come to be known as Metobolic Syndrome. Patients are subject not only to developing diabetes mellitus, but serious cardiovascular complications such as heart attacks and strokes. Management must not involve simply trying to lower the blood sugar, but also improving the many lifestyle factors that contribute to disease. Major changes are necessary in eating habits, exercise, stress reduction, and especially in understanding of the effect of food on health. Nutritional supplements also have great value in support of the diabetic patient, both by improving blood sugar control and by reducing end organ damage and preserving function of the kidneys, eyes, nervous and cardiovascular systems.

People should be aware of the fact that the benefit of medication on blood sugar control is often temporary. Over time, the medication becomes less effective as the individual sinks deeper into insulin resistance and overweight. Additional medications become necessary with their myriad side effects and ultimate ineffectiveness. Some of the diabetes medications actually result in weight gain, serving to worsen the overall problem. I rarely start a diabetic patient on medication during the first visit. I believe it is important for patients to appreciate the changes that can occur with lifestyle change and the initiation of nutritional supplements to enhance insulin effect.

Question: *The American Diabetic Association considers glycemic index as relatively unimportant in the selection of food for diabetics– do you agree?*

Answer: The glycemic index has great importance in choosing the proper diet. It does not however provide the only valuable guideline. High glycemic index foods should usually be avoided because they make blood sugar control more difficult, raise cholesterol and triglycerides, and increase weight. Not all high glycemic foods are forbidden. I think, for instance, that carrots provide great nutritional benefits and may be included in the diabetic diet if they are combined with other foods having a lower glycemic index. The nutrient content of foods is also an important factor, as is fiber content.

Question: *Do you wean type 2 diabetic off medication? If so, how and when?*

Answer: Yes. In taking a type 2 diabetic off medication, the blood sugar should be closely followed. Medication may gradually be reduced, provided the blood sugar does not rise excessively. I have seen many individuals reduce medications or eliminate them entirely while keeping the blood sugar in the normal range. When lifestyle changes in diet, exercise and nutritional supplementation are rapidly made, it is important to reduce the dosage of medication early. Otherwise the patient may be at risk of hypoglycemia, particularly if sulfonylurea drugs are used.

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seem to imply that these extracts may stimulate insulin secretion by increasing beta cell membrane permeability (43). Other research has also implicated gymnema in the suppression of blood glucose by inhibiting glucose uptake in the intestine (44). The current research and safety profile of gymnema extracts make it a leading botanical in the treatment of type 2 diabetes, and potentially, type I diabetes.

Bitter Melon

Bitter melon *(Momordica charantia)* is a tropical fruit that looks like a cross between a gourd and a cucumber. The fruit is eaten as a vegetable in many cultures, but has also been used for the treatment of diabetes by these same cultures. A large body of research now confirms the hypoglycemic effects of bitter melon in animal models, while only a few clinical trials have been done with diabetic patients. A trend in the animal research seems to imply the need for some insulin production, as NIDDM animal models responded to bitter melon treatment while IDDM models rarely did (45-49). This mechanism seems to be confirmed by *in vitro* evidence that shows protection of and increased numbers of pancreatic beta cells, and in some cases, an insulin-releasing activity (50-52).

Bitter melon extracts were also able to reduce oxidative stress and reverse the effects of chronic diabetes in an IDDM animal model (53). Additionally, bitter melon extracts show triglyceride and cholesterol lowering activity in diabetic animals (54), as well as non-diabetic animals fed cholesterol-rich diets (55). In an investigation of 4 traditional Indian anti-diabetic herbs *(M. charatia, Eugenia jambolana, Mucuna pruriens* and *Tinospora cordifolia)* in streptozotocin induced diabetic mice, bitter melon not only reduced plasma glucose levels more than the other herbs, but also significantly reduced renal hypertrophy compared to untreated diabetic controls (56).

Unfortunately, there are few published clinical trials using bitter melon in humans. In one case, 86% of the NIDDM patients experienced a hypoglycemic response to drinking an aqueous homogenized suspension of the vegetable pulp (57). This was similar

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to a report that 73% of type II diabetics responded to 2 oz of bitter melon juice (58). In both studies, response was measured by reduction in glucose tolerance after glucose challenge. These were not controlled trials, nor did they use extracts, making it difficult to assess what dose of the extract would best be used for diabetic patients. Various powdered extracts are now available and dosing is estimated at 750-1250 mg per day. More studies need to be conducted to confirm the efficacy of these extracts in humans, although the years of dietary use suggests that safety is unlikely to be an issue.

Fenugreek

The seeds of this Mediterranean spice have long been used for treating diabetes. It has been thought that the primary hypoglycemic mechanism is related to the large amount of water-soluble fiber content found in these seeds. Recently however, other hypoglycemic compounds have been isolated from fenugreek seeds and are being investigated for their role in treating diabetics (59-61). Most of the human clinical trials have been done with between 5 to 100 grams daily of fenugreek seed powder. This may be manageable for only a few patients who are willing to ingest these large amounts of powdered seed. Extracts may soon be used in clinical trials so that the non-fibrous hypoglycemic portions can be tested for effectiveness, dosing and safety.

Other Botanicals

It would be impossible to review all the other botanicals that have published research indicating potential use with diabetics, let alone cover all those for which traditional information is available. That said there are a few which are worth mentioning here. One of those is the herb Holy basil *(Ocimum sanctum* L.*)*. In animal studies and one human study, the leaves of holy basil had hypoglycemic activity. Unlike some of the other herbs above, holy basil lowered serum blood glucose in both normal and diabetic animals (63,64). A single-blinded placebo-controlled crossover study did show positive benefit in both fasting blood sugar and postprandial blood sugar in NIDDM patients consuming holy basil leaves (65). This may be an herb to watch as more research and extracts become available.

Another botanical worth considering is the multi-purpose milk thistle *(Silybum marianum L.)*, or more specifically the "seed" extract known as silymarin. Most often used for its liver specific effects, silymarin has shown promise in protecting chemically induced pancreatic damage (lipid peroxidation) in animal models of diabetes (66,67). Silymarin (600 mg/day) was also given to 30 insulin-treated type II diabetics suffering from alcohol induced lever cirrhosis. Both the treatment and the control group were treated with their previous standard therapy (68). In the silymarin group, their was a significant decrease in fasting blood glucose levels, mean daily blood glucose levels, glycosylated hemoglobin after only 4 months of treatment. At the same time there was a reduction in fasting insulin levels and stabilization of insulin need. While the data here is sparse, the overall safety and multiple other benefits gained by using silymarin may make it a beneficial addition to the natural treatment of diabetics.

Research from the University of Toronto has shown the potential use of American ginseng *(Panax quinquefolius L.)* in glycemic control (70-72). The use of as little as one gram of ginseng powder administered 40 minutes before a meal/glucose challenge was able to lower prostprandial glycemia. These effects were seen in normal as well as type 2 diabetic patients. Taken 40 minutes before a meal, ginseng may be helpful in the regulation of glycemic balance.

An extract of *Lagerstroemia speciosa* L., containing trace levels of corosolic acid, is currently being studied for its ability to lower blood glucose levels. A mechanism that allows glucose transport into cells, apparently without insulin, is being postulated. This mechanism seems to lower blood glucose regardless of diabetic status (at least for rats), and is deemed phyto-insulin by one company selling the extract.

Other botanicals include *Pterocarpus marsupium*, *Atriplex halimu*, and garlic *(Allium sativum)*, to name only a few that have published data. In the next 5-10 years, the growing desire to use natural remedies combined with the epidemic growth of syndrome X and diagnosed diabetes will cause the list of published botanical research reports to expand, and give the clinician and patient many more options.

Conclusion

Statistical research predicts that regardless of the type of practice, at least one in five individuals entering clinics in the United States has the metabolic precursors for insulin resistance and type 2 diabetes. The treatment and prevention of these disorders is both natural and eminently holistic. It was the intention of this review to give the clinician information on the many natural options available, and to act as a guideline for treatment and prevention. As each patient presents a different and unique history, different approaches may be applicable for their individual regimen. Balancing lifestyle and diet changes, as well as introducing nutraceuticals for prevention and treatment will be rewarded by slowing or even stopping potentially devastating outcomes– a reward worth the effort.

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