# Managing Blood Sugar

*There are many natural ingredients which purport to assist in the management of abnormal blood sugar. A review of the clinical evidence that supports (or refutes) the ability of these products to prevent diabetes.*

by Jay Udani

The obesity epidemic is foreshadowing the coming diabetes catastrophe, which has the potential to ruin lives and bankrupt medical systems. While medications are useful in managing the condition once it has manifested, food and dietary ingredients are powerful epigenetic modifiers which can prevent, manage, and possibly reverse the ravages of diabetes. There are many natural ingredients which purport to assist in the management of abnormal blood sugar and this article will review the clinical evidence that supports (or refutes) the ability of these products to benefit the millions of people who are at risk or already suffering from this dread disease. These products are seen as supplemental to standard pharmaceutical interventions and can be used responsibly alongside allopathic care.


## Staggering Growth

The accelerating growth rate of diabetes around the world is staggering. The WHO states that every minute, 6 people around the world die from diabetes or the complications of diabetes. The WHO also predicts that between 2000 and 2030 there will be an increase from 171 million to 336 million diabetics worldwide with the largest growth in the developing nations of India and China (150% and 163% increases respectively) (Hossain et.al. 2007).

The link with obesity seems clear enough, but the mechanisms are more complicated than originally thought. It appears that central adipose tissue (also known as white adipose tissue or WAT) is an endocrine, intracine and paracrine organ responsible for inflammation, coagulation, fibrinolysis, and atherosclerosis in addition to lipid storage and release (Lau et.al. 2005). This negative correlation between adiponectin levels and circulating inflammatory markers is found whenever there is excessive fat. Lipid engorgement of the visceral WAT triggers a cascade of changes with dire consequences. These changes include interruption of the production of adiponectin (which activates the PPAR system to increase insulin sensitivity), free fatty acid accumulation in other tissues and organs including the liver, and increased secretion of inflammatory and prothrombotic adipokines (Rajala et.al. 2003, Eckel et.al. 2002). The rapidly increasing WAT outgrows its blood supply and causes a relative hypoxia due to insufficient angiogenesis (Tataranni et.al. 2005). This in turn contributes to the accumulation of reactive oxygen species in the WAT and furthers the cycle of damage (Shigetada et.al. 2004).

## Inflammation Risks

People with higher levels of inflammation are significantly more likely to become diabetic when controlling for diet, genetics, and weight. Specifically, elevated levels of IL-6 are associated with a 2 fold increase in the risk of becoming diabetic, and increased CRP levels are associated with a 4 fold increase (Pradhan et.al. 2001).

The constant hyperglycemia also contributes to the oxidative stress and end organ damage. Markers of increased oxidative stress are positively correlated with the development of diabetic neuropathy and other complications of diabetes (Ziegler et.al. 2004).

Knowing the pathogenesis of the disorder, we can now focus on the ways to prevent and treat it. In addition to prevention, treatment strategies include raising adiponectin, increasing insulin sensitivity, reducing inflammation, reducing oxidative stress, enhancing glycaemic control, and reducing weight.

## Early Threat

Starting with prevention is key to the overall treatment strategy because the vascular damage to end organs can begin up to 7 years before the actual diagnosis of diabetes is made. There are several ingredients which can reduce the risk of diabetes, including magnesium. In a 15 year longitudinal study of 4,600 subjects, those who had the highest dietary magnesium intake were 31% less likely to become diabetic compared with those with the lowest levels of consumption (He et.al. 2008). The authors recommended that 400mg per day (320mg per day for females) be consumed and that it is preferable to get the magnesium from dietary sources including almonds, cashews, soybeans, spinach, avocado, beans and fish.

As plant starches account for the largest percentage of carbohydrate in the diet, and since these carbohydrates significantly impact the ability, the glycaemic index is a standard way to measure the glycaemic response to a particular food.

## Glycaemic Reduction

Three recent and rather large studies have demonstrated that people who follow a lower glycaemic diet significantly reduce their risk of developing diabetes compared with those who follow a high glycaemic diet. Collectively these studies followed 130,000 for between 5 and 8 years. The reduction in risk of becoming diabetic was between

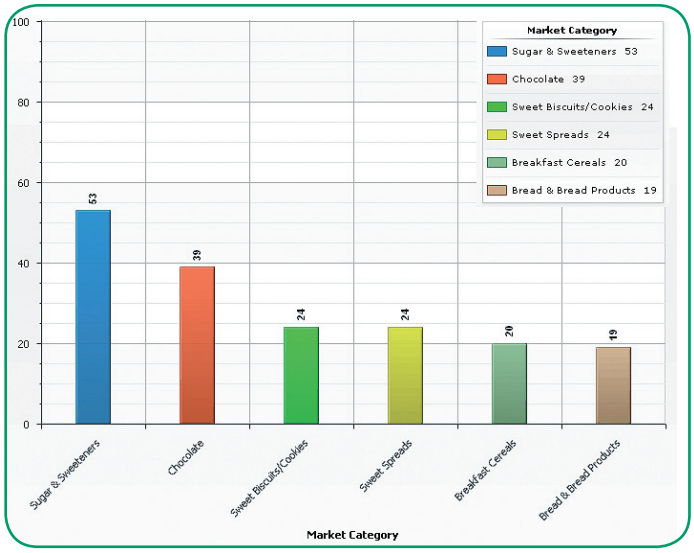
22% about 27% for those who followed the low glycaemic diets. (Krishnan et.al 2007, Villegas et.al. 2007, Schulze et.al. Arch int Med 2007). A meta-analysis of low glycaemic diets in diabetics showed an overall 0.4% reduction in HbA1c (a 3-month average of blood sugar control) compared to subjects who ate a high GI diet (Brand-Miller et.al. 2003). There are several ways to lower the effective glycaemic index of a food

A number of ingredients exist which can be added to foods to lower their effective glycaemic index. By including resistant starches or fiber (such as psyllium, blackgram fiber, barley or oat beta-glucan) to a high glycaemic food recipe, the rate of digestion and absorption of carbohydrates into glucose can be slowed and therefore the resulting insulin peak will be more gradual. This prevents the precipitous glucose drop which is the hallmark of the high glycaemic meal.

There are other dietary choices which impact the risk of diabetes. Foods which reduce the risk include polyunsaturated fats (40% reduction), vegetable oils (22% reduction), and coffee (30 to 60% reduction) (Van Dam et.al 2002, Tuomilehto et.al. 2004, Salazar-Martinez et.al. 2004, Hu et.al. 2001, Meyer et.al. 2001, Wang et.al. 2003). Foods which increase the risk of diabetes include saturated fat (2 to 3 times increased risk) and processed meats including hot-dogs and bacon (50% increased risk) (Hu et.al. 2001, Meyer et.al. 2001).

## Treatment Strategies:
### *Insulin and Glucagon*

Insulin is the primary hormone which controls blood sugar by increasing glucose transport, while stimulating the production of glycogen and fat. It is antagonised by glucagon which stimulates the breakdown of fat and glycogen into glucose. Ingredients which stimulate the production of insulin or mimic its effects can be effective in the regulation of blood sugar. These products include bitter melon (momordica charantia), gymnema sylvestre, cinnamon and green tea. Gymnema sylvestre has been shown to increase insulin secretion and it may contribute to beta-cell regeneration. Various components of gymnema have also been shown to temporarily block the ability of human taste buds to taste sweets. (Baskaran et.al. 1990). Momordica charantia (bitter melon) contain constituents with an insulin-like peptide called p-insulin (plant insulin). It is structurally similar to bovine insulin and may account for the properties seen with this plant. Bitter melon has been shown to affect glucose concentrations in humans, but most of the studies were uncontrolled and the dosages required were very high (up to 57g/day) (Sivastava et.al. 1993). Green tea was shown in a small pilot study to increase insulin sensitivity by 13% in healthy volunteers (Venables et.al. 2008) and when tested in a slightly larger study of 60 Japanese men, green tea was found to significantly reduce HbA1c compared with placebo (Fukino et.al. 2008). Cinnamon was shown in individual studies to be potentially helpful in modulating glucose and insulin, but when the results of the 5 randomised studies were combined into a meta-analysis (analysing 282 subjects) the authors concluded that there were no significant benefits on HbA1c or Fasting Glucose (Baker et.al. 2007).




Top markets for 'diabetic' products; (global Apr 09-Mar 10)
*Source: Innova Market Insights*

## Treatment Strategies:
### *Reducing Glucose Absorption*

Fenugreek (Trigonella foenum-graecum) is a soluble fibre, which appears to slow gastric emptying and may delay absorption of glucose from the gut (Sharma et.al. 1990). In animal studies, fenugreek has also been shown to increase the rate of insulin release. An extract of the white kidney bean (Phaseolus vulgaris) has been shown in multiple studies to reduce the rate of digestion and absorption of complex carbohydrates in healthy volunteers (Udani et.al. 2007). In addition, multiple studies have shown that obese subjects who consume this extract along with high-carbohydrate diets were able to lose weight compared with placebo (Celleno et.al. 2007).

## Treatment Strategies:
### *Mineral Co-Factors*

Diabetic and pre-diabetic subjects appear to suffer from various vitamin and mineral relative deficiencies which may be caused by excessive renal excretion of these co-factors. The ongoing insidious damage to the kidneys which is highly characteristic of the disease.

This damage leads to inadequate filtering functions and ultimately to the leakage of necessary vitamins and minerals into the urine. Replacing these vitamins and minerals appears to be significantly important in the overall management of diabetes and should not be ignored. Chromium is related to insulin sensitivity and a systematic review (Balk et.al. 2007) demonstrated that the effect of chromium on glycaemic control is limited to subjects with diabetes. Healthy subjects do not benefit from chromium supplementation.

A meta-analysis of 9 studies concluded that magnesium may lower fasting plasma glucose levels in diabetics (Song et.al. 2006). Selenium was once thought to be helpful, however a dermatology study found that supplementing with 200mcg of selenium increased the risk of becoming diabetic by almost 50%. Subsequent studies are ongoing, but at the moment caution is warranted when recommending selenium to people who are potentially at risk for diabetes.

## Treatment Strategies:
### *Antioxidants*

In addition to the oxygen poor visceral WAT, chronically elevated blood glucose


I Am Subzero Diabetic Vanilla Ice Cream (UK).

Source: Innova Market Insights

levels cause oxidative damage throughout the body resulting in increased circulating free radicals. Two small studies of vitamin E found that overweight subjects who took 1200 IU daily had improved insulin sensitivity (Lim et.al. 2004). A more recent study of a multi-component antioxidant (vitamin E, vitamin C, beta-carotene) for 8 weeks found significant reductions in insulin resistance as well as elevations in adiponectin (Vincent et.al. 2009).

Alpha lipoic acid has been shown in a meta-analysis of 4 RCTs to significantly reduce the symptoms of diabetic neuropathy, one the most painful and debilitating sequelae of diabetes (Ziegler et.al. 2004). The required dose is 600-1200mg/day and has been shown to improve the electrophysiologic tests of nerve conduction in these patients (Reljanovic et.al 1999). As the pathophysiology of this nerve damage may be related to hyperglycaemia induced free radical damage, it makes sense that significant antioxidant therapy may be able to reduce or potentially reverse some of these signs and symptoms.

## Treatment Strategies: *Raising Adiponectin Levels*

As reduced adiponectin leads to worsening of insulin resistance and inflammation, researchers have begun to look for ways to raise adiponectin levels. PPAR-γ agonists have been shown as a class to increase adiponectin levels, have a synergistic effect with insulin, and reduce inflammation in liver, adipose and vascular tissues (Gervois et.al. 2004, Hseuh et.al. 2003). There are several herbal products which have documented PPAR-γ activity, including bitter melon, mulberry leaf, Korean red ginseng, banaba, punica granatum, and turmeric. While these are exciting targets for future development, none of them have been shown to significantly raise adiponectin levels in human studies to date.

## Treatment Strategies: *Reducing Inflammation*

Whether inflammation is a cause or an effect of diabetes (or both) is not entirely clear, but reduction of inflammation is a valuable goal in these patients. There are several dietary supplements and herbal products which are known anti-inflammatories, including fish oil (omega 3 fatty acids), cat's claw, bromelain, ginger, boswellia, quercetin, evening primrose oil, borage oil, prickly pear cactus and turmeric. A full discussion of the data on these products is beyond the scope of this review. Interestingly, a study of 50 diabetic subjects receiving 2g/day of purified omega 3 fatty acids or placebo showed significant reductions in triglycerides but no changes in glucose, insulin, or total cholesterol (Shidfar et.al. 2008). There were several other studies of products which failed to improve inflammation or other diabetes related outcomes and these included cholecalciferol (Sneve et.al 2008), psyllium husk (King et.al. 2008) and plantago ovata husk (Salas-Salvado et.al. 2008).

## No Magic Bullet

While it is clear that none of these supplemental treatments are a magic bullet, there appears to be enough evidence to consider their supplemental use in the right population. Elucidating and understanding the underlying mechanism of action of these products is the key to selection of products which will be complementary to the activity of the standard pharmaceutical interventions which are already being used. Adding a product or ingredient which operates on the same pathway as a drug which is being taken simultaneously may not contribute additional benefit and thus picking products which activate different mechanisms of action are preferrable.♦

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