A Functional Medicine Approach to Diabetes
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Introduction

From a functional medicine perspective, treating type 2 diabetes means addressing its root causes—primarily insulin resistance and inflammation. More recent research suggests that biochemical pathway disruptions and lifestyle factors such as a lack of sleep and chronic stress may also be at play.

Studies have shown that insulin levels begin rising up to a decade before fasting blood glucose and hemoglobin A1c levels result in a diagnosis of diabetes, suggesting a prediabetic continuum that may not be captured by conventional lab work until it is too late.\(^1,2\)

Similarly, the role of inflammation in the development of diabetes has long been known. Elevated inflammatory markers such as C-reactive protein and interleukin-6 can predict the development of diabetes.\(^3,4\) Additionally, inflammation of the islet cells in the pancreas may contribute to their dysfunction.\(^5\)

A multi-pronged, personalized approach incorporating diet and lifestyle changes and targeted supplementation may help reverse the progression of the disease.

Testing
Insulin resistance can be measured using a variety of methods. The gold standard is a test called the hyperinsulinemic euglycemic clamp (HEC), which is invasive and costly, so surrogate measures are often used. These can be based on the results of an oral glucose tolerance test (OGTT) or fasting blood tests and include the homeostasis model of insulin resistance (HOMA-IR), the quantitative insulin sensitivity check index (QUICKI), and the fasting insulin resistance index (FIRI), which researchers have concluded correlate with the HEC.

Inflammation is most commonly measured using high-sensitivity C-reactive protein (hs-CRP), but other markers of inflammation include tumor necrosis factor alpha (TNF-α), interleukin-6, and ferritin. New inflammatory markers linked to the progression of diabetes are still being identified.

Problems with Current Treatments

The use of exogenous insulin in type 2 diabetes may actually worsen insulin resistance. In animal models, administration of insulin lowered blood sugar at first, but after 10 days of insulin therapy, the rats showed signs of insulin resistance and glucose intolerance. This may occur due to insulin’s inhibitory effect on AMP-activated protein kinase (AMPK), which modulates GLUT transporters that allow glucose into cells.

In contrast, the drug metformin works by suppressing hepatic glucose production and, to a lesser extent, by activating AMPK in the liver and muscle cells, which increases cellular glucose uptake. However, the benefits of metformin do not come without side effects. Gastrointestinal disturbances including gas and nausea are common, and long-term use can lead to deficiency in vitamin B12.

Diet

An eating pattern that targets the underlying root causes of diabetes should be implemented. Anti-inflammatory diets such as the Mediterranean diet have been shown to lower blood glucose, BMI, and cardiovascular risk factors in people with type 2 diabetes.

Diets high in plant phytonutrients are also beneficial. Anthocyanins have been shown to improve insulin resistance via multiple mechanisms, including increasing AMPK, increasing the number of GLUT receptors in cell membranes, and decreasing hs-CRP. Quercetin, a polyphenol found in onions, apples, green tea, and other fruits and vegetables has been shown to decrease inflammatory cytokines.

Low-carbohydrate diets are another strategy that may be effective in managing type 2 diabetes. A systemic review found that low-carbohydrate diets were at least as effective, and in some cases more effective, at achieving glycemic control, decreasing body weight, and improving cardiovascular risk markers as low-fat diets.

In one study, a low-carbohydrate (< 50 g/d), low–saturated fat diet was compared to a high-carbohydrate diet in people with type 2 diabetes for 1 year. The study found that
participants following the low-carbohydrate achieved greater improvements in lipid profile, better glycemic variability, and lower diabetes medication requirements compared with the high-carbohydrate diet group. Weight loss was similar across groups.\textsuperscript{15}

Finally, intermittent fasting may have a role in treating people with type 2 diabetes. Animal studies have suggested that intermittent fasting may improve insulin sensitivity and preservation of pancreatic beta cells.\textsuperscript{16} Additionally, intermittent calorie restriction may increase AMPK signaling and decrease inflammatory markers.\textsuperscript{17}

**Supplements**

There are several supplements that may useful in the treatment of type 2 diabetes by supporting glucose metabolism, improving insulin sensitivity, and reducing inflammation.

**Berberine:** Berberine is a plant alkaloid that may help increase glucose uptake into cells by upregulating AMPK and increasing the activity of GLUT transporters.\textsuperscript{19} Animal studies have shown that berberine lowers blood glucose and decreases weight in diabetic rats.\textsuperscript{19, 20} Furthermore, berberine has antioxidant and anti-inflammatory properties. Dosing for type 2 diabetes in studies ranges from 0.2 to 10 g/day.\textsuperscript{21}

**Chromium picolinate:** Chromium is a mineral essential for carbohydrate metabolism. Studies have shown it can lower fasting blood glucose and hemoglobin A1c in people with type 2 diabetes. Doses above 200 mcg/day may be more beneficial.\textsuperscript{22}

**Alpha lipoic acid (ALA):** ALA is an antioxidant that improves glucose uptake and has anti-inflammatory properties. It may be beneficial in preventing and treating diabetes and reducing the risk of complications such as retinopathy, neuropathy, and cardiovascular disease. Doses used in studies range from 300 to 600 mg.\textsuperscript{23}

**Cinnamon:** Cinnamon has been shown in studies to lower fasting glucose and hemoglobin A1c levels in people with diabetes. In a review of the research, doses ranged from 120 to 6000 mg a day, and all studies showed some glycemic control benefits. However, it appears that cinnamon alone may not be enough to achieve treatment goals recommended by the American Diabetes Association (fasting glucose < 130 mg/dL and/or HbA1c < 7.0\%). Therefore, it may best be used in combination with other treatments or as a culinary spice.\textsuperscript{24}

**Inositol:** Inositol may play key roles in the development of diabetes and its complications. Inositol is produced naturally in the body, with highest expression in the testes, ovaries, pancreas, heart, and placenta.\textsuperscript{25} Diets high in refined carbohydrates and vegetables are low in inositol. Additionally, inositol dysregulation has been identified in several conditions associated with glucose dysregulation, such as polycystic ovarian syndrome. Furthermore, high glucose levels inhibit inositol availability.\textsuperscript{26} Animal studies have suggested that inositol supplementation may reduce blood glucose and insulin resistance.\textsuperscript{27} A small study in humans showed a reduction in hemoglobin A1c with 1 gram of d-chiro-inositol plus 400 mg of folic acid daily for 24 weeks.\textsuperscript{28}
**Gymnema sylvestre:** Gymnema sylvestre is an herb with a long historic use in Ayurvedic medicine for diabetes. Studies have shown that it has hypoglycemic and anti-inflammatory effects and may work by stimulating pancreatic beta cells to increase insulin production. Small human studies have shown a reduction in postprandial glucose levels and hemoglobin A1c with a dose of 1 g/day.

**Bitter gourd:** Bitter gourd (Momordica charantia) is another herb that has been used in Ayurvedic medicine as well as in parts of Asia, South America, and East Africa. Studies have shown that it has hypoglycemic and lipid-lowering properties and may work by repairing damaged pancreatic beta cells to improve insulin production. It also may improve insulin sensitivity. In one study in 95 people with type 2 diabetes, bitter gourd (dosed at 2 grams or 4 grams a day) was found to show significant reductions in hemoglobin A1c and fasting plasma glucose, although the reductions were less than those seen with the diabetes medication glibenclamide. However, while the bitter melon groups showed improvements in cardiovascular risk factors including blood lipids, body weight, and blood pressure, people in the medication group showed worsening in these measures over the 10-week study.

**Other supplements:** Other supplements that may be of use in the treatment of diabetes include biotin and other B vitamins, vitamin D, magnesium, zinc, omega-3 fatty acids, mangosteen, curcumin, and fenugreek, although more research is needed. Additionally, nutraceuticals including resveratrol, quercetin, and EGCG may help activate the AMPK pathway, increasing glucose uptake through GLUT transporters.

**Lifestyle Recommendations**

Functional medicine practitioners take a holistic approach to wellness and often counsel patients on the importance of lifestyle changes for a whole-body approach to health. In the case of type 2 diabetes, exercise, sleep, and stress management are key.

**Exercise:** The link between physical activity and improvements in diabetes is well known. Furthermore, sedentary behavior has been strongly associated with the risk for developing type 2 diabetes. Studies have shown that regular physical activity improves insulin sensitivity by increasing AMPK activity. Additionally, exercise lowers inflammation in the body directly by lowering inflammatory cytokines and indirectly by effecting changes in body composition.

**Sleep:** Regular sleep may be linked with a lower risk for developing type 2 diabetes. Duration of sleep and risk for diabetes show a U-shaped relationship, with the most protective effects occurring with 7 to 8 hours of sleep per night. Too little or too much sleep was associated with a higher risk for developing the disease. Additionally, long-term sleep debt has been associated with long-term metabolic disruption and insulin resistance. In a prospective study in people with early type 2 diabetes, those with weekday sleep debt were 72% more likely to be obese at baseline. At 12 months, for every 30 minutes of weekday sleep debt, the risk for obesity rose 18% and the risk for insulin resistance rose 41%.
**Stress management:** Chronic stress has been linked to a higher risk for developing type 2 diabetes. In particular, high levels of night-time cortisol have been linked to higher fasting plasma glucose, hemoglobin A1c, and higher 2-hour plasma glucose. A flattened diurnal cortisol curve was also associated with a higher risk for developing the disease.\(^{39}\)

Yoga is one popular stress management technique that may show benefit for type 2 diabetes. In a systematic review and meta-analysis of studies on adults with type 2 diabetes, yoga significantly improved hemoglobin A1c levels as well as lipid profiles, BMI, blood pressure, waist-to-hip ratio, and cortisol levels.\(^{40}\)

Meditation has also been shown to improve glycemic control in people with diabetes. In a small study, participants who completed a Buddhist walking meditation on a treadmill were compared with those who walked on a treadmill without meditating. After 12 weeks, both groups showed significant reductions in fasting blood glucose, but reductions in hemoglobin A1c, blood pressure, and cortisol levels were seen only in the meditation group.\(^{41}\)

**Conclusion**

Type 2 diabetes is a multifactorial disease process stemming from insulin resistance, inflammation, sedentary behavior, sleep deficits, and chronic stress. Additionally, biochemical pathway dysregulation has been identified, especially a decrease in activation of the AMPK pathway, which mediates cellular glucose uptake in an insulin-independent manner. From a functional medicine perspective, dietary strategies, nutritional supplements, and lifestyle recommendations that encompass exercise, sleep, and stress management may all be necessary to improve markers of type 2 diabetes and decrease risk for complications.
References:


