Prevention and Treatment of Diabetes with Natural Therapeutics
Introduction
Diabetes, also known as sugar diabetes, is a disease in which blood sugar levels are abnormally high. In the United States, about one out of every 10 adults has diabetes or 26 million Americans. While diabetes is sometimes discussed as a single disease, there are actually several forms of diabetes. Each of these types has a different cause and typically affects different groups of people. For example, type I diabetes is caused by a problem in the pancreas, and organ that helps control digestion. People usually become aware of the fact that they have type I diabetes when they are children. Type 2 diabetes is more common and generally affects people later in life. The precise cause of type 2 diabetes is unknown. Pregnant women may develop a condition known as gestational diabetes, in which they have high blood sugar levels during and around the time that they are pregnant.

When someone has abnormal blood sugar levels, it can cause a number of problems, both over the near-term and over time. Very high levels of blood sugar can cause excessive thirst, the need to urinate frequently, nausea and vomiting, fatigue, confusion, and shortness of breath. When blood sugar levels are high for a long period—even only moderately high—this excess sugar can cause damage to various organs and tissues in the body. People who have poorly controlled diabetes may experience damage to their blood vessels and nerves, kidneys, eyes, and are at increased risk for heart attacks and stroke. Fortunately, the most common forms of diabetes are preventable. In people who already have diabetes, there are ways to control blood sugar and reduce the risk of short and long-term consequences.

A discussion of diabetes may seem complex, but it does not have to be that way. It does require, however, and understanding of certain terms and concepts. Once one understands these concepts, one can understand and manage diabetes.

Key Terms

Glucose: Glucose is simply sugar. While there are many types of sugar (e.g., sucrose, fructose), glucose is the most abundant sugar in the blood. Glucose is the type of sugar that is measured with blood tests. Perhaps you have heard of glucose meters or glucometers that allow people with diabetes to test their blood sugar level. Glucose is one of the main ways that the cells of the body get energy in the form of nutrition.

Insulin: Insulin is a hormone that is secreted by the pancreas. The pancreas secretes insulin in response to food entering the stomach/intestines. Glucose needs insulin in order to cross from the bloodstream into the cells. Without insulin, glucose stays in the bloodstream.

Synthetic (man-made) insulin: Synthetic insulin can be injected into the body as a treatment for high blood sugar. There are many kinds of synthetic insulin. The cells of the body react to synthetic insulin in the same way they would react to natural insulin—insulin causes glucose to enter cells.

Glucagon: Glucagon is a hormone that is secreted by the pancreas when blood sugar levels get too low. It causes the liver to release a small amount of sugar into the bloodstream.

Carbohydrates: Carbohydrates are one of three main nutrients (along with proteins and fats) that the body can use to produce energy. Carbohydrates include sugars and starches. Simple carbohydrates are small molecules, like glucose and fructose, in which one or two sugar molecules are bound together. Table sugar is an example of a simple carbohydrate. Complex carbohydrates are larger molecules and contain long chains of sugar molecules. Potatoes, beans, and whole wheat contain large amounts of complex carbohydrates.

Protein: Protein is made up of chains of amino acids and is an essential building block of our bodies. Sources of protein include meat, beans, and nuts. Protein can also be used by the body to produce energy for cells.

Fat: Dietary fat is an important nutrient and must be consumed in modest amounts. Fats and oils share the same molecular structure (i.e., lipids) but facts are solid at room temperature while oils are in liquid form. Fats are important for building cell membranes and brain cells, among other structures of the body. They are very powerful sources of energy since 1 gram of fat contains more than twice as much energy as 1 gram of carbohydrate.

Pancreas: The pancreas is an organ located just below the rib cage in the center of the body. It releases hormones into the blood such as insulin and glucagon. It also releases digestive enzymes into the small intestine. In type I diabetes, the pancreas does not produce insulin.

Liver: The liver is a large organ just under the rib cage on the right side of the body. Its main purpose is to detoxify and filter substances. It can also help regulate blood sugar levels and aid in digestion.

Kidney: The kidney is the primary organ for filtering the blood. Chemicals that the body does not need are filtered out or excreted by the kidney into the urine. Helpful molecules and cells (like red blood cells) are reabsorbed by the kidney or stay in the bloodstream. Under normal circumstances, glucose is reabsorbed by the kidney because it is an important source of nutrition for humans. However, in uncontrolled diabetes, there so much sugar in the bloodstream that it spills into the urine. This is why medical professionals can diagnose diabetes by running tests for glucose on the urine (e.g., urine dipstick).

Molecule: Generally speaking, a molecule is the smallest amount of a substance that is that substance. For example, H2O is a molecule of water, made up of two hydrogen atoms and one oxygen atom. A simplest sugar molecule (i.e., monosaccharide) is C6H12O6 or six atoms of carbon, 12 atoms of hydrogen, and six atoms of oxygen.

Cells: The body is made up of billions of cells. Every cell has certain responsibilities. For example, a muscle cell has to contract and a liver cell has to metabolize substances. Cells need energy in order to carry out their responsibilities. Most cells have the ability to turn nutrition (i.e., carbohydrates, proteins, and fats) into energy. In order for glucose to enter cells, insulin must be present.

Organs: A large collection of cells working together to perform certain tasks is called an organ. The heart, liver, and pancreas are examples of organs. Each of these organs is made up of countless cells.

Acute vs. Chronic: Acute and chronic are terms that describe the time over which events happen. An acute consequence of the disease is something that happens relatively rapidly. A chronic consequence of the disease develops slowly over
time. For example, a heart attack causes the acute symptoms of chest pain and shortness of breath. On the other hand, high blood pressure may develop over a period of years and slowly increase the risk of heart attack and stroke. High blood sugar levels that occur with diabetes can have both acute and chronic consequences.

**Metabolism:** Metabolism is the way in which the body breaks down or builds up molecules and makes them into more usable forms. One example of metabolism is the process in which a cell takes a molecule of sugar, breaks it down into smaller molecules, and produces energy. Another example of metabolism is the process by which the liver alters toxic molecules so they can be more easily excreted from the body.

**Genetics:** The way in which our genes (key parts of our DNA) affect our cells and organs and how genes are related to health and disease. Our genes are constant, but our behaviors and the environment can alter the degree to which our genes affect our cells and organs. In other words, someone may be genetically predisposed to developing type 2 diabetes, but that person can avoid developing the disease by taking the proper steps.

**Oxidation:** We need oxygen to survive, but certain forms of oxygen can be extremely harmful to cells. The oxygen in air is a very stable molecule (O2). When oxygen is in a “free radical” form, it will rapidly destroy cells any that it contacts. Some molecules create free radicals during metabolism. Fats are an excellent example. When fats go through metabolism (a process called lipid peroxidation) it creates oxygen free radicals, sometimes called reactive oxygen species. Antioxidants can protect cells from this oxidative damage by acting as a sponge for oxygen free radicals. Therefore, when oxygen free radical is formed it binds to an antioxidant instead of destroying a cell.

**Inflammation:** Inflammation is a large collection of cells from the immune system. Inflammation can be helpful when it occurs around the site of the bacterial infection. The immune cells can attack the bacteria, destroying them, and clearing the infection. However, inflammation is not helpful when it occurs without cause. Chronic inflammation may occur around joints, for example, causing arthritis.

**Autoimmune:** An autoimmune condition is when the immune system mistakenly attacks part of a person’s body thinking that it is a foreign invader, like a virus or bacteria. The immune system creates antibodies that target normal cells. These antibodies bind to the normal cells, telling the immune system to "attack here."

**Chelator:** A chelator is a molecule that tightly binds to an element in the body and filters it out in the urine, which reduces the level of that substance in the blood and body.

**Types of Diabetes**

**Type I Diabetes** - Type 1 diabetes used to be called juvenile diabetes or insulin-dependent diabetes (IDDM) because it occurs most often in childhood and is treated with insulin injections. Type 1 diabetes makes up between 5 and 10% of all cases of diabetes. Most cases of type 1 diabetes are due to an autoimmune condition. For reasons that are not fully understood, people who are genetically predisposed to developing type 1 diabetes may develop the disease if they experience the right environmental trigger or triggers. Current theories of the disease are that genetically predisposed individuals suffer some sort of viral illness or some other trigger that provokes an attack by the immune system. The immune system creates antibodies to fight the illness or insult. Unfortunately, these antibodies recognize cells in the pancreas that produce insulin. Therefore, instead of fighting an infection, the immune system attacks the pancreas and destroys the body’s ability to secrete insulin. Without insulin, glucose levels rise in the blood and cause problems discussed in greater detail in the Diabetes Complications sections.

**Type II Diabetes** - Type 2 diabetes is by far the most common form of diabetes. Between 90 and 95% of all cases of diabetes are type 2. Type 2 diabetes used to be called adult diabetes or non-insulin-dependent diabetes (NIDDM). These terms are no longer used because insulin can sometimes be used to treat type 2 diabetes and, unfortunately, children and teenagers are developing type 2 diabetes at an alarming rate.

Type 2 diabetes is not an autoimmune disorder, but the reason it occurs is not well understood. In type 2 diabetes, the pancreas continues to create and secrete insulin, but the cells do not respond to insulin normally. This process is called “insulin insensitivity,” which means the cells are no longer sensitive to the effects of insulin. Insulin sensitivity usually develops slowly over time. It may start with a condition called impaired glucose tolerance. Impaired glucose tolerance means that the body is unable to process dietary sugar as it once did. So after a meal containing sugar, the levels of blood sugar rise very high and stay high for an abnormally long period. Insulin is less effective, so it takes the cells a long time to absorb glucose from the bloodstream. As type 2 diabetes develops, people may experience impaired fasting glucose. This means blood glucose levels are high even when the person has not had a recent meal. Without effective management, both impaired glucose tolerance and impaired fasting glucose tend to get worse as type 2 diabetes progresses.

“Pre-diabetes” - A medical professional may tell a patient that they have “pre-diabetes.” Pre-diabetes means there is some amount of impaired glucose tolerance and perhaps impaired fasting glucose, but that it is not quite severe enough to be considered type 2 diabetes. People with pre-diabetes who do not take preventative steps usually end up developing type 2 diabetes at some point.

**Type 1.5 diabetes or latent autoimmune diabetes in adults (LADA)** - Infrequently someone will receive a diagnosis of type 1.5 diabetes also known as latent autoimmune diabetes in adults or LADA. The name type 1.5 diabetes is misleading because the disease is actually type 1 diabetes that is simply diagnosed later in life than usual. In LADA, the insulin secreting cells of the pancreas are slowly destroyed by an autoimmune condition. By contrast, in type 1 diabetes the pancreas’ ability to produce insulin is stopped rather rapidly. Unfortunately, LADA is often misdiagnosed as type 2 diabetes because it occurs most often in people above the age of 35.

**Gestational Diabetes** - Gestational diabetes is a condition that causes abnormally high blood sugars that first occurs when a woman becomes pregnant. Most cases of gestational diabetes resolve after delivery, though some women continue to have diabetes afterwards. Blood sugar levels should be controlled in women with gestational diabetes. As discussed in the Diabetes Complications section, elevated blood sugar levels can cause a variety of problems in pregnant women both for the mom and for the fetus.

**Idiopathic Diabetes** - A relatively small number of people with diabetes will have a condition known as idiopathic diabetes. Idiopathic diabetes is not an autoimmune disorder, so the immune system does not attack the pancreas. However, the pancreas does not secrete insulin as well as it should, so people with idiopathic diabetes need additional insulin. Very little is known about idiopathic diabetes, which means it can be difficult to manage and treat.

**Blood tests for diagnosing and managing diabetes**

**Glucose tolerance testing** - Glucose tolerance testing is a
way to test whether someone has insulin insensitivity or diabetes. It determines how the body reacts to a “meal” of glucose. The meal in this case is a beverage of concentrated glucose. The person being tested consumes the glucose beverage and blood samples are drawn once before and several times afterwards. In healthy people, glucose levels in the blood will increase and then return to normal rather rapidly. In people with insulin insensitivity or diabetes, the glucose levels stay high for a long period since glucose is not entering cells but is instead staying in the bloodstream. People with abnormally high levels of blood glucose during this test may be diagnosed with prediabetes or diabetes based on the measurements of blood glucose.

**Blood glucose testing** - The level of glucose in the blood can be measured by drawing blood, as it might be done in a hospital, or it can be tested using a finger stick and a blood glucose monitor. The blood glucose monitor allows people to test their blood glucose at home by pricking their own fingers and using personal devices. In fact, measuring blood glucose in this way is an excellent way for people with diabetes to monitor their disease.

Diabetes may be diagnosed, or strongly suspected, by results of blood glucose testing. If a blood glucose measurement is 126 mg/dL or higher in someone who has been fasting for at least eight hours (no calories at all) then the person qualifies for a diagnosis of diabetes. If the reading is above 200 mg/dL in someone who is not fasting, it is consistent with diabetes as well.

**Hemoglobin A1C** - The hemoglobin A1C test is a blood test that provides a measurement of your blood glucose level over the preceding three months. Blood glucose in the blood increases the hemoglobin A1C level, because additional sugar molecules stick to the hemoglobin. If someone has a hemoglobin A1C level above 6.5%, they have diabetes.

<table>
<thead>
<tr>
<th>A1C level</th>
<th>Average blood sugar level</th>
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<tbody>
<tr>
<td>5%</td>
<td>97 mg/dL/L9%</td>
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<tr>
<td>6%</td>
<td>126 mg/dL/L0%</td>
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<tr>
<td>7%</td>
<td>154 mg/dL/L1%</td>
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<tr>
<td>8%</td>
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If you have diabetes or prediabetes, your doctor will likely test your hemoglobin A1C level every three months to see how tightly your blood glucose was regulated.

**Lipids** - Because diabetes and heart disease are so closely related, anyone with insulin insensitivity or diabetes should have routine blood lipid testing. Lipid testing includes cholesterol and triglyceride levels in the blood. Furthermore, cholesterol testing includes total cholesterol, low-density lipoprotein (LDL, “bad” cholesterol), and high-density lipoprotein (HDL, “good” cholesterol). The most recent recommendations for lipid levels come from consensus guidelines from the major medical societies including the American College of Cardiology, the American Heart Association, and the National Heart, Lung, and Blood Institute (ATP-IV). The ATP-IV considers diabetes a risk factor for developing cardiovascular disease just like smoking and high blood pressure are risk factors. However, diabetes is a greater risk for heart disease and smoking.

**C-reactive protein** - C-reactive protein (CRP or hsCRP for high sensitivity C-reactive protein) is a measure of inflammation in blood vessels that is associated with heart disease. This blood test provides an excellent measure of future cardiovascular disease risk in people with existing heart disease; however, this test is of limited usefulness in people without diagnosed heart disease.

**Controlling diabetes**

The main goal of therapy in diabetes is to control blood glucose levels by keeping them as normal as possible. Countless studies have determined long-term complications from diabetes can be minimized or avoided by keeping blood sugar levels near normal, which can be done through a variety of methods including diet, exercise, prudent lifestyle choices, and regimen of supplements and medical treatments.

People with prediabetes and diabetes are strongly encouraged to measure their blood glucose level frequently, which can be done several times a day with glucose monitors or by measuring hemoglobin A1C every three months. These measurements allow the patient to detect successes and shortcomings and make changes to their management approach and treatment regimen.

You may have heard of the term “tight control” or “tight regulation” in diabetes care. These terms refer to a regimen designed to keep blood sugar levels as close to the normal range as possible. While tight control of diabetes is a good goal, it brings with it the risk of making blood sugar levels too low, which opens the door to a different set of problems. The ideal management approach keeps glucose levels in the blood relatively low but not too low as to cause problems.

**Acute effects of diabetes**

The damaging effects of diabetes occur in direct relation to the level of blood glucose. These symptoms happen rapidly or acutely. The type/severity of the effect changes with the degree of blood glucose abnormality. In other words, the more abnormal the blood glucose (higher or lower), the more severe the diabetes symptom is.

**Symptoms of mildly elevated blood sugar** - People who have mildly high levels of sugar in the blood (readings between 200 mg/dL and 350 mg/dL in adults) will usually experience several effects of excess blood sugar, which include increased thirst and fluid consumption, increased urination, weight loss, fatigue, and increased appetite. Having too much sugar in the blood convinces the body that it is dehydrated, so the affected person drinks more fluids and this increased fluid consumption means that they urinate more frequently. However, glucose will also be present in the urine, which tends to pull more fluid out of the body, which further increases dehydration, thirst, and the need to urinate.

It may seem confusing or even paradoxical that people with high blood sugar will be hungry and lose weight. However, with diabetes, the cells are not getting the sugar that they need—it stays in the bloodstream. The cells are actually craving nutrition—even starving. Therefore, the body becomes hungry and the person with uncontrolled diabetes loses weight.

**Symptoms of moderately elevated blood sugar** - When blood sugar levels get higher than 350 mg/dL (240 mg/dL in children), additional symptoms of diabetes start to emerge. These symptoms include extreme thirst, dizziness, blurred vision, hot/dry skin, hot flashes/flushes, and possibly drowsiness. The person’s heart rate and breathing rate will increase and they may experience abdominal pain and vomiting.

**Symptoms of severely elevated blood sugar** - The most feared and severe acute consequences of having high blood glucose are diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic
state (HHS). These conditions are very similar to one another and can even occur at the same time. The differences between the conditions are only important for medical professionals—patients simply need to understand both are severe, result from very high levels of blood glucose, often require emergency medical attention, and may lead to coma or death. Unfortunately, most people with type 1 diabetes first realize they have the disease because they develop diabetic ketoacidosis. Symptoms of these conditions include increased urination, increased thirst, nausea/vomiting, and weight loss. The weight loss may be difficult to detect since symptoms generally developed over a period of one to three days. As blood sugar levels continue to rise, it negatively affects brain function causing lethargy, weakness, confusion, breathing problems, seizures, and possibly coma. Treatment of these conditions includes intravenous treatment with insulin, fluids, and electrolytes. In more serious cases, patients may need to have a breathing tube until blood sugar levels can be brought under control.

Symptoms of too little blood sugar - It may seem odd to discuss the symptoms of too little blood sugar or hypoglycemia when discussing the disease of abnormally high blood glucose. However, people who are on treatments for diabetes may experience times in which blood sugar drops too far. This is especially a concern for people who receive insulin therapy or certain oral hypoglycemic drugs that can cause hypoglycemia. Unfortunately, the symptoms of having low blood sugar are similar to those that occur when blood sugar is too high. Symptoms of hypoglycemia include anxiety, tremors, sweating, hunger, and the feeling of “pins and needles.” Heart rate and blood pressure may also be higher than normal. Since the symptoms of high and low blood sugar are very similar, the best course of action is to take a blood glucose measurement—a finger stick test with a blood glucose monitor. The treatments for high and low blood sugar are very different, and the right treatment should be given based on the measurement rather than a sign or symptom.

Chronic complications of diabetes
The complications of diabetes develop over time and tend to get worse the longer the patient has diabetes. The following complications often take years to emerge, but they tend to occur in relation to chronic blood glucose levels. People with diabetes who keep their blood sugar levels near normal may never develop these complications or may only develop mild versions of them. People who have chronically elevated blood sugars—poorly controlled or uncontrolled diabetes—may develop these complications relatively quickly and tend to experience severe complications.

Damage to small blood vessels—Microvascular disease - Almost all blood vessels in the body are considered small blood vessels. These small blood vessels are particularly vulnerable to high levels of glucose in the blood. In fact, most complications that arise from chronically high levels of glucose in the blood, namely nerve problems, kidney problems, eye problems, and poor wound healing are believed to be caused by damage to small blood vessels. Fortunately, this damage—also called microvascular disease—can be minimized by keeping blood sugar levels near normal. The more closely that blood glucose levels stay at normal or slightly high levels, the less likely it is that one will develop microvascular disease.

Damage to large blood vessels—Macrovascular disease - Poorly controlled or uncontrolled diabetes over a long period also puts large blood vessels at risk. The risk of coronary heart disease, heart attack, stroke, and death by a cardiovascular cause is higher in someone with diabetes and the risk increases proportionally to the level of blood glucose.

In other words, higher levels of blood sugar correspond to higher risks of heart disease and stroke. Unlike small vessel blood disease, tightly controlling blood glucose does not seem to reduce the risk of macrovascular disease as much as one might expect. Therefore, people with diabetes should also focus on heart health in addition to managing their diabetes, since simply having diabetes is an independent risk factor for developing cardiovascular disease.

Nerve problems—Diabetic neuropathy - Nerves in the feet and hands need a good supply of blood in order to function properly. The microvascular disease that occurs in diabetes harms small blood vessels and eventually harms nerve endings. Over time, it is quite common for the nerves of the feet, initially, and hands, later in the disease, to be affected by high levels of blood glucose. High blood sugar is not the only risk for developing diabetic neuropathy. Other risk factors include high cholesterol, high triglycerides, high blood pressure, and smoking.

Diabetic neuropathy develops slowly. It may occur so subtly in the beginning it can only be detected by performing neurological tests. It usually starts with a loss of the ability to sense vibration in the very tip of the toes. Over time, other forms of sensation are lost, including the sense of pain, light touch, and temperature. This loss affects ever-increasing areas of the foot; starts in the toes then progresses into the feet and then up the leg. Other, more subtle neurological issues can occur as well. Diabetic neuropathy can also be painful. The pain may feel like “pins and needles” or even a constant, burning pain. While these symptoms may improve as blood glucose levels improve, diabetic neuropathy is more often permanent. Therefore, it is far better to avoid developing this condition than trying to treat it after it occurs.

Foot and skin problems - Diabetes can be particularly damaging to the feet. People with diabetes tend to heal slowly, because the healing process requires a good blood flow to the injured area. Because small blood vessels have been damaged, healing can be delayed so minor cuts can last for a very long time, which is especially troubling for people who have nerve problems in the feet. The feet lack the ability to sense objects and painful stimulation, so people may suffer small injuries to their feet that they do not even notice. Since the person is not aware of the injury it is left unattended, heals slowly, and is very likely to become infected since bacteria love the high levels of sugar in the blood. Bacteria also use sugar as food. People with diabetes must take especially good care of their feet and should see a foot specialist regularly.

Kidney problems—Diabetic nephropathy - The kidney is the main filtration system for the blood and when it is working properly, it does an excellent job of keeping protein, blood cells, and glucose in the bloodstream while filtering out waste and toxins. During the course of diabetes, the kidney loses its ability to perform these functions. People with diabetic nephropathy tend to “spill” protein in their urine and, over time, they may also lose red blood cells. The protein and blood in the urine are usually not visible to the naked eye, but they can be detected with urine analysis. Needless to say, losing protein and blood in the urine is unhealthy and can cause serious problems over time.

Eye problems—Diabetic retinopathy - The layer of cells in the back of the eye called the retina is critical for vision. A number of very small, very delicate blood vessels supplies the retina. Chronically high blood sugar can harm the small blood vessels in a variety of ways. Over time, that damage can lead to
blurred vision and even blindness. The rate of blindness in people with diabetes is an astonishing 25 times higher than it is in the general population. Diabetes is the most common cause of blindness for middle-aged individuals in the United States.

Problems with the digestive system——
Gastroparesis - The stomach and the intestines are not simply tubes through which food flows. These organs contract to propel food along the digestive system. Nerves send signals to the muscles around these organs to contract and relax in an organized manner. As many as 20 to 40% of people with diabetes develop problems with this process and suffer from a condition known as gastroparesis.8 This means food and beverage that enters the stomach does not pass normally into the intestines. This can cause heartburn, stomach pain, indigestion, and acid reflux.

Metabolic syndrome - Metabolic syndrome is a collection of risk factors and findings that tend to occur in the same individuals and increase the risk for diabetes and cardiovascular disease. Metabolic syndrome is also known as insulin resistance syndrome and syndrome X. One definition of metabolic syndrome is someone who has three of the following five traits: abdominal obesity, high blood triglycerides, low HDL cholesterol, high blood pressure, and high fasting blood glucose. There are several definitions developed by different professional organizations, but the important thing to note the relationship between diabetes, obesity, high cholesterol, high blood pressure, and cardiovascular disease. Most people agree these risk factors should be targeted as a group for the prevention and treatment of both diabetes and heart disease.

Type I diabetes risk factors and prevention
Perinatal factors - Factors occurring at the time of childbirth
In a study of 892 children with diabetes and 2291 children without the disease, researchers have found there is a small increase in the risk of type 1 diabetes if the mother of the child is older than 25 years or had preeclampsia (high blood pressure and protein in the urine that can lead to seizures/eclampsia), or if the child had respiratory disease or jaundice at the time of birth. The risk was also significantly higher if there was some incompatibility in ABO blood group between the mother and the child. Conversely, low birth weight and short birth length appear to be protective factors.9 Unfortunately, few of these factors can be controlled or modified.

Viruses - Animal studies have revealed viruses that can destroy insulin-producing cells in the pancreas or trigger an autoimmune attack against these pancreatic cells.10 For instance, a virus called Coxsackie B may create immune responses that are damaging to pancreatic cells. In children with newly diagnosed type 1 diabetes, 39% had immune responses to Coxsackie B virus while children without diabetes have immune response rates of about 6%.11 Moreover, Coxsackie virus antibody titers—a marker of immune response to the virus—were significantly higher in pregnant women whose children subsequently developed type 1 diabetes, compared with pregnant women whose children did not become diabetic.12 The same study also found viruses affecting the digestive system—enteroviral infections—were nearly two times more common in siblings who developed type 1 diabetes compared to non-diabetic siblings.12 Autoimmune diabetes and other autoimmune diseases may occur 5 to 20 years after infection with rubella—German measles.13

Childhood immunization - Childhood immunization of
prevalence of diabetes than Mexican Pima Indians. This difference is presumably due to large differences in diet, exercise, and other lifestyle factors.

Perinatal factors (factors occurring at the time of childbirth) - There seems to be an inverse correlation between birth weight and type 2 diabetes. In a study of nearly 70,000 women, those who weighed more at birth were less likely to develop type 2 diabetes than those who had lower birth weights. In separate studies, those who are considered underweight at birth but then became overweight in middle age had the most severe insulin resistance and highest risk for type 2 diabetes out of any group studied. Taken together, these studies suggest individuals who had a low birth weight should probably pay particular attention to excessive weight gain in middle age. On the other hand, individuals who had a very high birth weight, a birth weight above 5 kg or 11 pounds, had an increased risk for developing type 2 diabetes later in life. However, since we cannot control our birth weight and can only control our current weight, it seems prudent that maintaining a good weight regardless of your birth weight is the best approach for preventing diabetes.

Obesity and physical activity - There is an extremely strong link between obesity and the development of type 2 diabetes. Likewise, there is a strong inverse correlation between physical activity and diabetes. In other words, most people who develop type 2 diabetes are overweight or obese and have lower than average physical activity. Obesity and inactivity are considered risk factors for diabetes and diabetes-related cardiovascular disease. Obesity makes the cells of the body resistant to the effects of insulin. Moreover, obesity makes the cells of the pancreas less able to detect the presence of glucose in the blood, which means even though blood levels of glucose are high, the pancreas does not react appropriately by secreting a sufficient amount of insulin. Fat tissue may release hormones that adversely affect the way the body processes glucose and fat, namely leptin, adiponectin, and tumor necrosis factor-alpha. These molecules contribute to insulin resistance and impair insulin action. Fat tissue also releases various chemokine molecules, which attract inflammatory cells and form reactive oxygen species. Not only does this increase overall inflammation in the body but may also contribute to insulin insensitivity. Several other molecules such as plasminogen activator inhibitor 1, resistin, retinol-binding protein 4, interleukin-1 beta, uncoupling protein 2, and obestatin may play a role in the development of or protection against diabetes and are influenced by the amount of fat on the body.

Physical inactivity, independent of obesity, contributes to the development of type 2 diabetes. Physical activity on the other hand, not only reduces the risk of diabetes but it also improves health-related quality of life, physical functioning, mental health scores, feelings of vitality, and psychological well-being. When muscles are routinely used, they make better use of circulating insulin and therefore are better able to absorb glucose. Even modest exercise can be helpful. Brisk walking between 30 and 60 min. a day reduces the risk of developing type 2 diabetes by 30%. Physical activity may also be protective against gestational diabetes.

Fortunately, even very obese patients who managed to lose weight were able to restore the way their muscle cells respond to insulin. In people with type 2 diabetes, short-term exercise programs improves insulin sensitivity. Weight loss can dramatically change the amount of medications and/or insulin required to treat the disease. People with type 2 diabetes who exercise after eating can reduce their need for diabetes medications. Type 2 diabetes is perhaps the most responsive to changes in weight, particularly body fat composition. In fact, weight loss surgery—bariatric surgery—may result in remission of type 2 diabetes though long-term benefits depend on sustained weight loss. In summary, while inactivity and obesity are risk factors for type 2 diabetes, physical activity, and weight loss can be preventative or curative.

Conventional medications for diabetes

The goals of conventional medicines in the treatment of diabetes are to reduce the amount of glucose in the blood and increase the amount of glucose entering cells of the body. Each class of medications achieves these goals in different ways. Almost everyone who receives an initial diagnosis of type 2 diabetes will be started on an oral medication called metformin. Metformin decreases the amount of glucose the liver makes and improves insulin sensitivity throughout the body. These two actions help keep blood sugar low while feeding the cells with the glucose it needs. Metformin may cause nausea, diarrhea, gas, and bloating. The drug may also interfere with the body’s ability to absorb vitamin B12 and folic acid. Metformin may not be appropriate in people with kidney, liver, or heart disease or heavy drinkers of alcohol. Metformin usually reduces hemoglobin A1C levels by about 1.5%-46, which means if your hemoglobin A1C is higher than 9% your physician will likely suggest another drug besides metformin because metformin will not be able to reduce hemoglobin A1C to target levels—usually 7% or 7.5%.

While metformin is the standard first-line agent for the treatment of type 2 diabetes, there is considerable variety in choices of second line agent depending largely on patient preferences and physician experience. The most commonly prescribed second line therapy is a drug class known as a sulfonylurea. The prototypical drug in this class is glipizide or glyburide. Sulfonylureas are sulfite drugs so if you have a sulfite allergy, you should tell your physician before starting this drug. Sulfonylureas are taken orally and work by increasing the amount of insulin secreted by the pancreas. Unlike metformin, sulfonylureas can cause dangerously low blood sugar called hypoglycemia. The symptoms of too little blood sugar are described above but include sweating, feeling shaky, feeling hungry, and anxiousness. If these feelings occur, it is important to have a rapidly acting carbohydrate available, such as fruit juice, which will raise glucose back to a safe level in the blood. Sulfonylurea drugs can and often do cause weight gain, which can be troubling for patients. Sulfonylureas are very potent at the beginning of type 2 diabetes, but tend to lose their effect as the disease progresses.

Another second line antidiabetic drug class are the thiazolidinediones. Examples of thiazolidinediones are pioglitazone (Actos) and rosiglitazone (Avandia). These drugs are taken orally and work by improving insulin sensitivity, which means insulin works better on cells to permit the entry of glucose. Thiazolidinediones may cause hypoglycemia, but the risk of hypoglycemia with these drugs is less than that of sulfonylureas. Common side effects include weight gain and the accumulation of fluid in the ankles and feet. People who take thiazolidinediones are at an increased risk of developing or exacerbating congestive heart failure, macular edema, bladder cancer, and bone fractures.

Alpha-glucosidase inhibitors, like acarbose (Precose) and miglitol (Glyset), interfere with the body’s ability to absorb carbohydrates in the gut, which means carbohydrates consumed in the diet simply pass through the gastrointestinal tract.
While this helps lower blood sugar levels, the drug also substantially increases abdominal bloating, flatulence, and diarrhea. These side effects generally limit the use of these drugs. When these drugs are used, alpha-glucosidase inhibitors are taken orally, three times a day, at the beginning of each meal.

Meglitinides such as repaglinide (Prandin) and nateglinide (Starlix) are quite similar to sulfonylureas but are not sulfa drugs, so people with a sulfa allergy can use them. Unfortunately, meglitinides are much more expensive than sulfonylureas and must be taken orally with each meal. Side effects include weight gain of hypoglycemia, the less profound hypoglycemia than sulfonylureas. DPP-IV Inhibitors are a relatively new form of oral anti-diabetes medication that increases the amount of insulin released by the pancreas in response to a meal. While these drugs do not cause hypoglycemia or weight gain, they are very expensive and since they are new, not much is known about their long-term side effects. Nevertheless, these drugs may increase the risk of heart failure, pancreatitis, and pancreatic cancer. Examples of DPP-IV Inhibitors include sitagliptin (Januvia), saxagliptin (Onglyza), and vildagliptin (Galvus).

Glucagon-like peptide (GLP)-agonists, such as exenatide (Byetta) and liraglutide (Victoza), are administered via injection rather than orally. GLP-agonists may be used when glucose or hemoglobin A1C levels remain high after one or two oral anti-diabetes drugs have been prescribed. These drugs do not cause a dangerous drop in blood sugar or weight gain. In fact, they actually help promote weight loss. On the other hand, people taking these medications must experience injections and complain of nausea, vomiting, and diarrhea. These drugs may or may not cause pancreatitis, which is a painful and sometimes deadly inflammation of the pancreas. GLP-agonists tend to be expensive compared to most oral diabetes medications.

Insulin, which is available only by injection or intravenously, can mimic the effects of the body's own insulin produced by the pancreas. There are a variety of insulin types sorted by the length of time they act in the body, specifically rapid-acting (e.g., insulin lispro a.k.a. Humalog), short-acting (regular insulin), intermediate-acting (insulin NPH), or long-acting insulins (e.g., insulin glargine a.k.a. Lantus®). Insulin is a critical treatment for people with type 1 diabetes. These individuals are reliant on insulin injections. In type 2 diabetes, however, insulin is usually reserved for patients who have tried to use oral hypoglycemic medications for some time. Using insulin is a big commitment because it requires that patients check their blood glucose several times a day using a finger stick and blood glucose monitor. Patients must also determine the amount of insulin they need based on their glucose readings. Most insulin regimens can be quite complex and challenging for patients. Simpler regimens, such as the use of long acting insulin, do not always deliver tight glycemic control. In addition, the risk of hypoglycemia is very high with insulin. Weight gain is also extremely common, especially with shorter-acting insulins.

**Dietary management of diabetes**

**Glycemic Index and Glycemic Load** - The glycemic index of foods is a mathematical formula based on the reaction the food has on blood glucose levels within two hours of consumption. In other words, the higher and faster a food raises blood sugar levels, the higher the food's glycemic index is. A candy bar has a rather high glycemic index while oatmeal as a relatively low glycemic index. However, this glycemic index is based solely on the type of food. Glycemic load converts the glycemic index into a different number that takes total carbohydrates, dietary fiber, and net carbohydrates into account. The glycemic load is a better way to determine the effect of food on blood sugar levels.

Carbohydrate-containing foods that have low or below average glycemic load or glycemic index may reduce the risk of several chronic diseases including type 2 diabetes, which suggests mostly eating foods that raise blood sugar slowly rather than rapidly helps prevent developing type 2 diabetes and other chronic diseases. One of the biggest complaints about Western diets is the glycemic load of most prepared and commonly eaten foods is high. The glycemic load of white bread, soft drinks, white flour pastas, and most processed foods eaten in Western societies is high. Recent research, collected from 24 separate clinical trials, has determined there is a dose response relationship between high glycemic load diets and type 2 diabetes. People who have a diet in which the average glycemic load is above 95 g per 2000 kcal consumed—kcal is what is commonly considered a calorie—are at significantly increased risk of developing diabetes regardless of other risk factors. Likewise, consuming foods with a lower glycemic load are protective against developing type 2 diabetes. In fact, many diabetic diets are based on minimizing glycemic load.

As a rule of thumb, it is better to eat breads and pastas made from whole grains than from highly processed carbohydrates, such as white flour. In a study of more than 160,000 women, those who ate two or three servings of whole grains each day were 30% less likely to develop type 2 diabetes than women who ate processed carbohydrates. In women who ate even more servings of whole wheat products (4 to 5), the decreased risk was approximately 50%.

**Advanced glycation endproducts (AGE)** - In patients with diabetes, strict control of blood sugars can help reduce many complications—but not all diabetes-related complications. For instance, tight glucose control can help reduce the risk of eye disease and kidney disease but has no perceptible effect on macrovascular or large blood vessel disease, which means there is some other cause of complications besides elevated blood sugar. One likely culprit is advanced glycation endproducts or AGEs. AGEs are a byproduct of food that is processed at high temperatures. AGEs are also pro-oxidant molecules, the opposite of antioxidants. These molecules negatively affect the structure of a variety of proteins and cells and they react with other molecules to produce other, stable, damaging molecules.

The foods with the highest AGE content include in decreasing order: high fat foods, high protein foods (meat and meat substitutes including tofu), and finally carbohydrate-dense foods. Of the high fat foods, spreads including butter, cream cheese, mayonnaise, and cooking oils have particularly high AGE content. For the high protein foods, the method of cooking was particularly important in determining AGE content with oven frying, deep frying, and broiling producing the highest AGE content in food. Steaming, boiling, poaching, and microwaving produced lower AGE content in foods. Processed foods, i.e. boxed and pre-cooked foods, have the highest AGE content for carbohydrate dense foods. The lowest AGE foods included low-fat dairy, vegetables, and fruits.

Recent evidence suggests food-related AGEs can initiate oxidative stress and create reactive oxygen species in humans before diabetes starts. In other words, the oxidative damage from these chemicals precedes the onset of diabetes. Studies in mice have shown if you restrict AGEs from their diet yet keep
the same number of nutrients and calories, you can reduce inflammation improve the animals host defenses, prevent the development of diabetes, reduce complications that occur in the blood vessels and in the kidneys and extend the normal lifespan.\textsuperscript{54} Trials in patients have shown similar results—restricting AGEs reduced oxidative stress and improve markers of insulin sensitivity.\textsuperscript{55}

**Medical nutrition therapy** - Medical nutrition therapy is a highly specific dietary and exercise regimen tailored to the individual needs of the patient with diabetes. The goals of medical nutrition therapy in diabetes are to achieve and maintain excellent blood sugar control, healthy levels of cholesterol, triglycerides, blood pressure, body weight, and physical activity. Medical nutrition therapy can be an effective intervention. Studies have shown hemoglobin A1C can be reduced by 2% in people with recently diagnosed type 2 diabetes and 1% in patients with long-standing diabetes.\textsuperscript{56,57}

Medical nutrition therapy encompasses five main measures including 1) calorie intake and expenditure, 2) increasing physical activity and weight loss, 3) stable amounts of carbohydrates in the diet from day to day, 4) well-balanced nutrition, and 5) meal planning and timing to correspond with expected hunger and anti-diabetic medications. Calorie intake and expenditure usually requires some sort of calorie counting program. The patient must count the calories consumed along with the type of nutrition consumed (e.g., carbohydrates, fats, proteins, etc.) but also the number of calories burned through basal metabolic rate and physical activity. Physical activity should be tailored to the patient’s preferences while attempting to reach targeted weight goals. Patients pursuing medical nutrition therapy will likely be trained in determining glycemic load of foods and recording those values for their meals on a daily basis. Eliminating one food group (e.g., Atkins diet or no-carb diets) is not consistent with medical nutrition therapy. Patients are instead encouraged to take in reasonable numbers of all major nutrition sources such as low glycemic index carbohydrates, unsaturated fats, and sources of lean protein along with adequate vitamins and minerals. Lastly, it is important for maintaining relatively constant levels of blood glucose rather than sharp spikes and deep valleys, which is especially true in patients who are taking insulin or even oral anti-diabetic drugs.

**Garlic** - Garlic (Allium sativum) has been used for centuries in Persia and surrounding areas to treat sugar diabetes. Garlic appears to work by lowering blood glucose. In a study of 60 people with type 2 diabetes, the addition of garlic tablets to the standard anti-diabetic therapy regimen had significantly lower fasting blood sugar levels after six months of treatment than those in the control group (standard medical care with no garlic supplements).\textsuperscript{58} Interestingly, LDL and total cholesterol levels are decreased and HDL-cholesterol levels increased in the treatment group.\textsuperscript{58} A separate clinical study using time-released garlic powder tablets had the same effects on fasting blood glucose.\textsuperscript{59} Is unclear whether garlic in the diet has the same beneficial effects on fasting blood glucose, though it appears higher levels of garlic (garlic supplements) are required for the observed clinical effect.

**Good fats, bad fats, and Omega-3 Fatty Acids** - For most people, the types of fat consumed influence the risk of cardiovascular disease. Less well known is the fact: “good” fats help prevent type 2 diabetes\textsuperscript{60} and “bad” fats increase the risk.\textsuperscript{61} Good fats are high in polyunsaturated fats as would be found in nuts and the oils of certain vegetables. Bad fats are trans fat and saturated fats, including partially hydrogenated vegetable oil. Omega-3 fatty acids like those prevalent in fish oils do not directly prevent the development of type 2 diabetes nor do they help in regulating blood glucose. However, Omega-3 fatty acids are an important part of the diabetic diet because of the greatly increased risk of cardiovascular disease for people with diabetes. Supplementation with 1,800 mg daily of the omega-3 fatty acid, eicosapentaenoic acid (EPA) decreases the progression of atherosclerosis in people with type 2 diabetes.\textsuperscript{62}

**Fiber** - Dietary fiber (a.k.a. roughage) is a substance that is not digested or absorbed. Instead, it stays in the digestive tract until it is passed in the feces. Dietary fiber is helpful in maintaining bowel regularity and may bind unwanted substances, passing these substances with bowel movements rather than being absorbed into the body. Dietary fiber is divided into soluble and insoluble forms. Wheat dextrin is an example of soluble fiber while cellulose as an example of insoluble fiber. Fiber is found naturally in the “coverings” of foods like the outer layer of wheat grain called wheat bran and in the skins/peels of fruits and vegetables, among other places. Various dietary supplements are sources of dietary fiber, such as psyllium husk.

Since most convenience foods and prepackaged meals are highly refined they lack much of the dietary fiber found in natural foods. For example, white rice is a polished form of brown rice in which the fibrous germ and bran coating has been removed. Western cultures tend to prefer white rice to brown rice, which extends into most other staples; we prefer white bread to whole wheat bread, we prefer white flour pasta to whole wheat pasta, and we prefer our fruit in juice form rather than with skins and seeds and stems. With the exception of vegetarians and vegans, few Americans get the recommended daily amount of fruits and vegetables. As a result, most Americans do not get nearly the amount of fiber recommended by the US Department of Agriculture (25 to 35 g per day). Moreover, these fiber-reducing alterations (e.g., brown rice polished into white rice) greatly increase the glycemic index of food.

Low fiber diets increase the risk of colon cancer, heart disease, bowel irregularity, diverticulitis, metabolic syndrome, and type 2 diabetes.\textsuperscript{63,64,65} Conversely, high-fiber diets appear to be relatively protective against these diseases.\textsuperscript{51} Dietary fiber supplements can help reduce glucose levels in the blood in response to glucose tolerance testing, even in people without diabetes.\textsuperscript{66,67} Dietary fiber may also help lower fasting blood glucose. In a trial of 30 men with mildly elevated blood glucose and abdominal fat, the addition of 7.5 g of dietary fiber each day for 12 weeks lowered body weight, body mass index, and fasting blood glucose.\textsuperscript{68} In a trial of 44 patients with type 2 diabetes, an additional 10 g per day of soluble fiber improved various measures of metabolic syndrome after 4 to 6 weeks of taking the fiber. Participants who took the fiber had reduced waist circumference, hemoglobin A1C, urinary protein excretion, and fatty acid levels in the blood.\textsuperscript{69} While fruit juice may be a concern to people with type 2 diabetes, eating fruit in its natural state is still acceptable. In a trial of 63 people with newly diagnosed type 2 diabetes there is no difference in hemoglobin A1C, body weight, or waist circumference whether they were told to restrict fruit intake or not.\textsuperscript{70} Presumably, the fiber contained in the fruit makes up for the simple sugars in the fruit.

**Alcohol** - Consuming alcohol in moderation apparently reduces the risk of heart disease, but it may also reduce the risk of type 2 diabetes. Small amounts of alcohol improve insulin sensitivity in cells.\textsuperscript{71} One alcoholic beverage per day in women and two beverages for men decrease the risk of developing diabetes.\textsuperscript{72,73,74,75} On the other hand, excessive
amounts of alcohol can increase the risk for type 2 diabetes. People who drink alcohol should do so in moderation and those who do not drink alcohol should probably not start just to decrease the risk of diabetes.

Red meat and processed meat - In a study group of nearly half a million individuals, researchers identified about 30,000 who developed type 2 diabetes during the study period. By comparing the diets of those who did and did not develop diabetes, they determined a daily serving of red meat increase the risk of developing type 2 diabetes by 20%. Processed red meat such as hot dogs, sausages, and bacon, increase the risk of diabetes by over 50% when eaten daily. Conversely, reducing the amount of red meat in the diet can reduce the risk.

Trace Minerals

Chelation - Disodium EDTA is a chelator that binds to calcium, magnesium, lead, cadmium, zinc, iron, aluminum, and copper is sometimes used as a treatment for atherosclerosis. In a recent clinical trial, 1,708 people with a previous heart attack were randomly assigned to treatment with chelation therapy including disodium EDTA or placebo. Treatment with EDTA significantly reduced the risk of a death, recurrent heart attack, stroke, the need for coronary artery stent or balloon procedure, and hospitalization for angina. Importantly, there were also small but nonsignificant reductions in each of these endpoints individually with EDTA treatment. However, when investigators specifically looked at individuals with a prior heart attack and diabetes, EDTA was particularly effective at reducing the cardiovascular events listed. While the authors conclude this study is not sufficient to support the routine use of EDTA for chelation, the study did identify diabetic patients as being particularly helped by this treatment approach.

Chromium - In the 1950s, researchers discovered a substance from the kidney of pigs they called “glucose tolerance factor” because it could lower blood glucose levels when administered to rats. Years later, this glucose tolerance factor was actually discovered to be the element chromium (Cr). Several studies show chromium deficiency causes impaired glucose tolerance and abnormalities in blood lipids. Chromium supplementation significantly reduced plasma glucose concentrations during a glucose tolerance test and significantly improved the body’s ability to use glucose. It also eased the symptoms of diabetic neuropathy and improved glucose intolerance. Taking chromium early in the course of diabetes therapy can reduce the degree of insulin resistance. On the other hand, some clinical trials have not shown an effect of chromium on diabetes or insulin sensitivity. Supplementation with 25 or 200 µg of chromium did not affect glycemic control or insulin sensitivity in diabetic patients. Yet an equally recent study found 100 to 200 µg of chromium yeast had a beneficial effect on fasting plasma glucose and hemoglobin A1C. These beneficial effects went away after a “washout period” in which chromium yeast supplementation was stopped for some time.

Chromium is found in reasonable amounts in foods such as grains, cereals, vegetables, and fruits. Unfortunately, humans do not readily absorb chromium from the gut and most is excreted through as waste. Other trace metals can affect the absorption of chromium. Specifically, people who are deficient in zinc or iron tend to absorb chromium more effectively. Conversely, magnesium, calcium, and aluminum salts can interfere with chromium absorption. Vitamin C appears to enhance absorption of chromium.

Vanadium - Vanadium is a trace element in a variety of foods and in water, air, and soil. It rarely exists as a pure metal, but is likely combined with oxygen and hydrogen in a related form, such as vanadate, H2VO4-. It is unclear whether vanadium is critical to biological processes, but humans probably do require vanadium in small amounts. People usually consume between 6 to 18 µg of vanadium each day. The safe upper limit of vanadium is 1800 µg though it is not clear when toxic effects start to occur. Since accumulates vanadium in the body with long-term use, toxic effects of this trace mineral may appear over time as has been reported in animal studies.

Vanadium is able to reduce blood glucose levels in diabetic rats and in humans with type 2 diabetes. Vanadium appears to act like insulin by increasing glucose absorbance into cells, the precise mechanism is unclear. One problem with studies examining vanadium in diabetes is at the doses administered are orders of magnitude higher than what is considered safe. For example, people with type 2 diabetes experienced a significant decrease in hemoglobin A1C and an increase in insulin sensitivity after taking vanadium, but the dose required to observe this effect is between 150 and 300 mg or 150,000 to 300,000 µg. one every one taking the 300 mg dose experienced diarrhea and other unpleasant gastrointestinal symptoms. While vanadium may be able to reduce blood glucose and act like insulin does, the doses required to achieve this effect may not be low enough to avoid toxic effects from vanadium.

Selenium - Selenium participates in a number of biological processes. Seafood, Brazil nuts, red meat, and organ meats such as liver and kidney are rich in selenium. The selenium content of vegetables depends greatly on the amount contained in the soil. More than half of the selenium that we eat is absorbed in the gut. In fact, the selenium connected to other amino acids such as methionine and cysteine is absorbed readily. It is important to note while selenium supplements exist, there are serious health consequences for selenium levels that are too low and too high. Selenium deficiency can lead to a specific form of heart disease called Keshan disease, but this only occurs in diets that are essentially devoid of selenium. Too much selenium may cause nausea, vomiting, diarrhea, hair loss, peripheral changes in the nerves, and confusion. The recommended dietary allowance of selenium is 55 µg per day and should be limited to 400 µg per day at most.

Much of what we know about selenium and diabetes comes from work in animals. Selenium can mimic the effects of insulin and can reduce blood glucose levels however too much selenium in the diet can actually exacerbate type 2 diabetes. Given that selenium may be toxic in high concentrations and may potentiate type 2 diabetes when taken in excess, it seems prudent for individuals to not over-supplement with selenium. While selenium supplementation may be helpful in people who have low selenium levels, supplementation to achieve higher than normal levels of selenium in the blood may not be helpful.

Copper - About 60% of dietary copper comes from vegetable products in the US. An additional 20% comes from grains and legumes while the final 20% comes from meat, fish, and poultry. Copper is important for the function of several enzymes including those defending against reactive oxygen species. There is some evidence to suggest removing copper from the blood through copper chelation may be a viable treatment for
Copper chelation may be a viable way to remove copper from the blood in patients with type 2 diabetes; however, this approach is not yet considered standard medical care. Clinical trials of copper chelation are ongoing.

Zinc - Zinc was identified as a distinct element in the early 16th century, but it would take 400 years to realize it was essential in biological organisms including humans. Even today, zinc deficiency is an important medical issue in children and young adults, mostly in developing countries. Severe zinc deficiency can cause failure to grow, impaired immunity, decreased ability to resist infections, skin disease, and sexual problems. It is quite possible subclinical zinc deficiency (i.e., mild deficiency that does not create easily perceptible signs or symptoms) contributes to a number of diseases such as Crohn’s disease, cystic fibrosis, sickle cell disease, and diseases of the liver and kidneys. Zinc levels can be determined by a blood test and values below 60 mcg/dL are considered abnormally low. On the other hand, zinc supplementation is relatively safe because ingestion of up to 10 times the RDA of zinc is 15 mg of zinc per day.97 Interestingly, the intestinal absorption of copper is inhibited by zinc. Therefore, high doses of zinc can lead to copper deficiency; however, reducing copper may actually be beneficial in type 2 diabetes.

Zinc appears to mimic the effects of insulin when it is applied to pancreatic cells or given to animals with diabetes.98 Zinc and zinc-containing supplements may be helpful in the management of type 2 diabetes. In a randomized, double-blind clinical trial, 75 individuals with type 2 diabetes and peripheral neuropathy were treated with either zinc containing supplements or placebo. While the supplements did not change glycemic control after four months of treatment, people who took zinc experienced improvements in their peripheral neuropathy.99 Zinc may also have a direct effect on blood glucose concentrations. In a study that examined 14 clinical trials including almost 4000 participants, those who were treated with zinc supplements experienced significant decreases in fasting blood glucose levels and a small but not statistically significant decrease in hemoglobin A1C.100 When participants with chronic metabolic diseases such as type 1 diabetes type 2 diabetes, metabolic syndrome, and obesity were grouped, zinc supplementation cause an even greater reduction in blood glucose.100 A clinical trial is ongoing to determine whether zinc supplementation can help improve features of prediabetes and perhaps prevent the disease from becoming type 2 diabetes.101 Importantly, the effects of zinc on glycemic control and other features of diabetes may take six months or more to see.102

Magnesium - People with diabetes tend to have lower magnesium levels in their blood than healthy individuals.103 Magnesium deficiency is particularly common in children with type 1 diabetes,104 which may be because people with type 1 diabetes consume insufficient amounts of magnesium in their diet.105 In fact, most Americans consume less magnesium each day than the recommended dietary allowance. It is more difficult for patients to control their diabetes when they have low levels of blood magnesium.106,107 Low levels of magnesium in the blood increase the risk for diabetic foot complications.108 Likewise, dietary supplementation with magnesium may help prevent macrovascular complications from diabetes, which do not respond to glycemic control alone.109 On the other hand, supplementation with magnesium may improve insulin sensitivity and insulin secretion in people with type 2 diabetes.110 A study of 62 subjects with type 2 diabetes who also had low magnesium levels showed by correcting the deficiencies in these subjects with oral supplementation of a magnesium chloride solution, insulin sensitivity was improved, as were HbA1C and fasting glucose measures.111 Magnesium supplementation may help prevent people from developing cardiovascular disease or type 2 diabetes. Nearly 40,000 American women were followed as part of the women’s health initiative. People with higher levels of magnesium consumption lower rates of type 2 diabetes and vice versa.112 In other words, magnesium was protective against type 2 diabetes. These results have been confirmed in a meta-analysis of studies including over half a million patients.113 In a group of 2,582 adults who had prediabetes—i.e., impaired fasting glucose, impaired glucose tolerance, or mild insulin resistance—those who had the highest magnesium intake had a 37% lower risk of developing type 2 diabetes compared to those with the lowest intake.114

Vitamins

Vitamin A and Beta-carotene - Beta-carotene is a precursor to vitamin A and may be abnormally low in people with diabetes. One hundred and seven patients with type 2 diabetes were compared to 143 people without diabetes. Beta-carotene levels in the blood were significantly lower in people with diabetes though retinol (vitamin A) levels were normal.115 This finding has since been confirmed.116 Despite many studies showing beta-carotene deficiencies in people with type 2 diabetes, supplementation with 50 mg beta-carotene in a randomized clinical trial with over 20,000 patients showed no effect of beta-carotene supplementation on the development of type 2 diabetes.117

Thiamine (Vitamin B1) and Benfotiamine - Thiamine, sometimes called vitamin B1, is important for glucose metabolism within cells and for the proper functioning of insulin secreting cells in the pancreas. As with beta-carotene, thiamine concentrations are significantly lower in people with diabetes than in healthy individuals.118,119 There are number of biological links between thiamine and diabetes and diabetes complications. The high content of thiamine in fiber is believed to explain in large part why increased fiber intake can improve glucose tolerance.120 A group of 24 people with newly diagnosed type 2 diabetes who had not yet started in medical therapy was given 150 mg of oral thiamine each day for one month. This dosage significantly decreased fasting blood glucose and leptin, which is a hormone involved in obesity.121 Benfotiamine, a drug that is very closely related to thiamine, was able to reduce hemoglobin A1C levels after 45 days of treatment in 22 diabetic patients.122 In the same study, this thiamine precursor helped improve symptoms of pain and discomfort with diabetic neuropathy and electrophysiological measurements of nerve function, as well.122 In a separate study of 165 patients with diabetic neuropathy, benfotiamine at a dose of 600 mg per day improved symptoms of neuropathy after six weeks of treatment.123 On the other hand, high-dose benfotiamine (300 mg/day) treatment for 24 months and did not improve nerve function in 59 patients with type I diabetes.124

Vitamin B6 - Several studies have shown vitamin B6 levels are abnormally low in many people with diabetes, though usually in those with diabetic neuropathy.125,126,127,128 Clinical studies on the effect of vitamin B6 supplements have shown varying results.129,130,131 Vitamin B6 treatment may be particularly helpful in gestational diabetes.129,130 In a multicenter, randomized, double-blind, placebo-controlled
Vitamin B12 is particularly important for the function of nerve cells and is necessary for the production of red blood cells. Conventional medical treatments for diabetes (e.g., metformin) can lead to vitamin B12 deficiency, especially in people with diabetes. Vitamin B12 deficiency can result in the appearance of painful muscle cramps, paresthesias, and the ability to walk improved markedly, and restless leg syndrome disappeared.

**Vitamin B12** - Vitamin B12 is essential for the normal function of the nervous system and the production of red blood cells. It is also necessary for the metabolism of fat and the production of DNA. Vitamin B12 deficiency can cause anemia, weakness, fatigue, and tingling sensations in the hands and feet. In severe cases, it can lead to irreversible nerve damage.

**Biotin (Vitamin B7)** - Biotin plays a critical role in the way in which glucose is metabolized within cells. Biotin participates in gluconeogenesis, which is the creation of glucose from smaller molecules within cells, e.g., lactate, pyruvate. Thus, biotin can help cells use alternate sources of energy besides glucose to power cells. This effect was exemplified in a small clinical trial in which seven people with type 1 diabetes were temporarily taken off insulin therapy and either given and 16 mg of biotin a day or placebo. Fasting blood glucose levels rose significantly in patients receiving placebo, as expected. However, in those receiving biotin, blood levels of glucose decreased. Most studies of biotin in diabetes treatment have focused on type 2 diabetic patients. Biotin supplementation combined with chromium supplementation appears to improve the way in which glucose is processed by cells. Forty-three people with type 2 diabetes who were receiving treatment but had poor glycemic control were randomly assigned to a group given 600 mcg of chromium and 2 mg of biotin per day or placebo in addition to their standard diabetes medicines. After four weeks, people treated with supplements had a significantly improved oral glucose tolerance test and had more favorable triglyceride and HDL levels.

Biotin has also been used to treat diabetic neuropathy. Three patients with severe diabetic peripheral neuropathy received 10 mg/day of biotin intramuscularly (IM) for six weeks, followed by 10 mg IM three times a week for six weeks, then 5 mg/day orally. The treatment duration ranged from 64 to 130 weeks. Within 4-8 weeks of the start of treatment, painful muscle cramps, paresthesias and the ability to walk improved markedly, and restless leg syndrome disappeared.

**Vitamin B12** - Vitamin B12 may be of particular concern to people with diabetes because vitamin B12 deficiency occurs as a consequence of aging but is also a side effect of certain conventional medical treatments for diabetes (e.g., metformin). Vitamin B12 is particularly important for the function of nerve tissue, including the nerves of the eye in the limbs. Vitamin B12 injections (50 or 100 mcg added to a daily insulin injection) was able to reverse diabetic retinopathy (diabetes-related eye disease) in type I diabetes patients. Indeed, it appears vitamin B12 deficiency may, in part, predict the onset of diabetic retinopathy. Levels of vitamin B12 in the blood negatively correlate with the occurrence of diabetic retinopathy. In other words, as vitamin B12 deficiency became more severe in diabetic patients, the likelihood or incidence of diabetic retinopathy increased. While it is unclear whether supplementing vitamin B12 above normal levels can help treat diabetic retinopathy, research suggests vitamin B12 deficiency should be treated aggressively, especially in people with diabetes.

Vitamin B12 has also been used to treat diabetic neuropathy. Several studies from the 1950’s show vitamin B12 supplementation improves neuropathy, however, work in this area has not been pursued heavily in the past half-century. In one study, 12 patients received an injection of 15-30 mcg/day of vitamin B12 by injection for 7-14 days, followed by 15-30 mcg, 1-2 times a week. Seven patients had complete or near complete remission of the neuropathy and three had partial improvement. The response appeared to depend more on the frequency of the injections than on the amount of each individual dose. Vitamin B12 was shown to be more effective than the tricyclic antidepressant, nortriptyline, at improving the neuropathy symptoms of pain, tingling, burning, freezing, stabbing, and electrical sensations in 100 patients with painful diabetic neuropathy.

**Vitamin C** - Vitamin C or ascorbic acid is a water-soluble vitamin found in citrus fruits. It is also reasonably potent antioxidant and may be protective against oxidative damage in addition to directly improving diabetes. People with vitamin C deficiency often have diabetes that is difficult to control with medications. In fact, researchers found not only did vitamin C deficiency correlate with poor glycemic control, but that supplementing with vitamin C and restoring it to normal levels in the blood normalized blood glucose as well. A study of 56 outpatients with type 2 diabetes showed 2 grams of vitamin C per day improved glycemic control, fasting blood glucose levels, cholesterol and triglyceride levels. In a double-blind, placebo-controlled clinical trial of 70 patients with type 2 diabetes, 12 weeks of vitamin C supplementation along with standard metformin therapy in both groups reduced fasting blood glucose, postmeal blood glucose, and hemoglobin A1C levels significantly more than placebo.

A randomized, double-blind study of 30 patients with type 2 diabetes found supplementation with 1,250 mg of vitamin C per day combined with vitamin E supplementation slowed the progression of diabetes-related kidney disease. People with type 2 diabetes have, on average abnormally low vitamin C levels when compared to healthy people. This vitamin C deficiency also corresponds to gum disease, namely periodontitis and gingivitis. Moreover, supplementing the diet with vitamin C improves gum disease in these patients.

**Vitamin D** - Vitamin D is a hormone—rather than a true vitamin—that regulates the flow of calcium into the body and into bones. Recent research suggests vitamin D is also important for the way the body regulates glucose levels. Vitamin D deficiency is relatively common in people with type 1 diabetes. Likewise, proper functioning of vitamin D and calcium is necessary for the pancreas to secrete insulin. Conversely, reversing vitamin D deficiency can help improve lower blood glucose and improved insulin secretion in people with type 2 diabetes. Vitamin D levels may predict who will go on to develop type 2 diabetes. When researchers reviewed 19 studies they found people who had the highest levels of vitamin D (over 25 ng/mL in the blood) had a 43% lower risk of developing type 2 diabetes than those in the lowest vitamin D group (less than 14 ng/mL). Supplementation with large amounts of vitamin D (50,000 units of vitamin D3 orally per week for eight weeks) resulted in improvements in fasting plasma glucose and insulin levels in diabetic patients. The same dose of vitamin D supplementation reduced systolic blood pressure (top number) by 11 points and diastolic blood pressure (bottom number) by four points after 12 weeks of therapy in 60 people with type 2 diabetes. In a separate study, 50,000 units of vitamin D3 given to pregnant women with gestational diabetes lowered fasting blood glucose and insulin levels compared to those taking placebo. Women also saw improvements in total and LDL cholesterol with vitamin D supplementation.

Since vitamin D is a fat-soluble vitamin, it tends to accumulate in the body over time. Too much vitamin E can cause dehydration, vomiting, decreased appetite, fatigue, muscle...
weakness, and abnormally elevated levels of calcium in the blood. The safe upper level of vitamin D intake is 10,000 IU per day.\textsuperscript{154}

**Vitamin E** - Vitamin E is a fat soluble vitamin and relatively potent antioxidant. Results of clinical studies of vitamin D in the treatment of diabetes have varied considerably. A double-blind, placebo-controlled study, administration of 900 mg/day of vitamin E for four months to type 2 diabetes patients significantly improved glucose tolerance.\textsuperscript{155} Vitamin E supplementation with 800 IU per day for one month improved the function of insulin-secreting cells in the pancreas, increased insulin levels in the blood, and may have decreased insulin resistance in 40 patients with type 2 diabetes.\textsuperscript{156} Another double-blind, placebo-controlled trial, however, did not show any improvement in glycemic control.\textsuperscript{157} It is unclear why there are discrepancies between clinical trials on vitamin E supplementation.

### Supplements and Natural Products

**Coenzyme Q10** - Coenzyme Q10 (CoQ10) is a critical protein in the mitochondria or power plants of the cell. In addition to its energy-generating properties, CoQ10 is a potent antioxidant. The molecule continuously converts between oxidized and reduced states in its energy-making process. Thus excess CoQ10 can interact with reactive oxygen species and neutralize them, thereby preventing damage to cells and substances inside of cells.\textsuperscript{158} In a small study of nine people with type 2 diabetes on conventional medication for the disease, researchers found individuals who consumed an oral dose of 200 mg of CoQ10 for 12 weeks had significant improvements in hemoglobin A1C insulin levels.\textsuperscript{159} Daily supplementation with 200 mg of CoQ10 also reduced hemoglobin A1C levels in a larger, 74 patient, double-blind clinical study and was also found to significantly decrease blood pressure.\textsuperscript{160} CoQ10 is better known for its ability to improve blood vessel health (endothelial function). Forty people with type 2 diabetes and abnormal blood cholesterol levels received 200 mg of CoQ10 for 12 weeks, which improved blood flow to the brachial artery (the major artery in the upper arm) suggesting CoQ10 can improve blood vessel function.\textsuperscript{161} In a study of 64 type 2 diabetes patients, CoQ10 improved glycemic control, total cholesterol and LDL cholesterol but did not affect triglyceride, HDL, or fasting blood glucose levels.\textsuperscript{162}

**Carnitine** - Carnitine is not exactly a vitamin nor is it an essential amino acid, but it is related to both types of molecules. Carnitine is important for fatty acid metabolism in mitochondria. The biologically active form is L-carnitine. Carnitine levels are abnormally low in people who have cholesterol abnormalities\textsuperscript{163} presumably because pools of carnitine are depleted because of excess fat metabolism. Carnitine prevents the progression of blood vessel lesions in animals with elevated cholesterol levels in the blood.\textsuperscript{164} Carnitine supplementation (2 g daily for three months) reduced LDL cholesterol levels, triglycerides, and other molecules associated with the oxidation of LDL compared to placebo in people with type 2 diabetes.\textsuperscript{165} A separate clinical trial found carnitine supplementation (1 g three times a day for 12 weeks) reduced fasting blood glucose but somewhat inexplicably increased the level of triglycerides in the blood.\textsuperscript{166} This increase in triglycerides may have been due to a statistical anomaly, because a systematic review of four trials including almost 300 patients with type 2 diabetes showed triglyceride levels are not significantly affected by carnitine supplementation.\textsuperscript{167} In fact, the studies agreed carnitine lowers fasting blood glucose, total cholesterol, it LDL levels.

**Carnosine** - Carnosine—not to be confused with carnitine—is a dipeptide (two amino acids) that is found in high concentrations in muscle and brain tissue. Carnosine is a free radical scavenger and has antioxidant properties. Additionally, carnosine is a chelator of divalent metal ions such as copper, iron, and zinc.\textsuperscript{168,169} Oral administration of carnosine in rats was able to protect small blood vessels in the eye against persistent high blood glucose levels sustained over six months experimentally.\textsuperscript{170} Studies in obese rats also showed carnosine-supplemented drinking water (30 mg per kilogram) reduced blood pressure, cholesterol, and triglyceride levels in the blood.\textsuperscript{171} The supplement also appeared to delay the progression of kidney disease in these rats. Topical carnosine i.e., carnosine applied directly to the skin, was able to speed up wound healing in diabetic mice.\textsuperscript{172} Carnosine may be able to prevent diabetes induced blood vessel disease.\textsuperscript{173} Carnitine and related compounds were able to suppress the formation of advanced glycation endproducts (AGEs), which may be helpful against AGE-related diabetes complications.\textsuperscript{174}

**N-Acetyl Cysteine (NAC)** - N-Acetylcysteine or NAC is a precursor to a molecule called glutathione. Glutathione is one of the major waste-removing molecules in the body. When certain molecules need to be excreted from the body, glutathione binds with it so that it is more easily filtered and excreted by the kidney in the urine. As such, glutathione is a very potent antioxidant. Supplementation with NAC is a way to rapidly replenish stores of glutathione. NAC has many medical uses from reversing acetaminophen overdose to protecting the kidneys from iodine-containing contrast used in CT scans.

In a clinical trial, NAC was able to restore glutathione concentrations in platelets and was ultimately able to reduce the risk of thrombosis or clotting in patients with type 2 diabetes.\textsuperscript{175} Long-term supplementation with NAC protected diabetic animals from developing retinopathy.\textsuperscript{176} In diabetic rats, NAC was able to potentely block oxidative damage in all organs tested including heart, lung, liver, and kidney.\textsuperscript{177} This antioxidant effect appears to occur in humans as well. Ten people with type 2 diabetes and 10 normal subjects were given a high glucose meal and glucose was tested along with other parameters in the blood. The high glucose meal created an increase in markers of oxidation in people with diabetes but not in healthy subjects. However, the administration of NAC reduced oxidative stress and protected blood vessels.\textsuperscript{178}

**Alpha Lipoic Acid** - Alpha-lipoic acid (ALA) is a potent antioxidant and participates in the conversion of glucose into energy. Both of these functions may be helpful in diabetes. ALA improves insulin sensitivity.\textsuperscript{179} Twelve patients with type 2 diabetes were given oral ALA in a dose of 600 mg twice a day for four weeks and compared to 12 healthy individuals. Circulating insulin was significantly increased in people with diabetes compared to when they started the treatment. In fact, the levels were approximately the same as those in healthy individuals. Thus, even after relatively short treatment with ALA, the supplement was able to normalize insulin sensitivity.\textsuperscript{180} ALA may also function like insulin in the body—like an insulin-mimetic.\textsuperscript{181} A group of 57 type 2 diabetes patients received either 300 mg of ALA a day or placebo and were followed for eight weeks. The ALA-treated group had significantly lower levels of fasting blood glucose and blood glucose after eating—post-prandial glucose.\textsuperscript{182} In another study, 22 obese individuals with impaired glucose tolerance were given 600 mg per day of ALA intravenously.
After two weeks, insulin sensitivity improved rather dramatically in ALA-treated patients and markers of cholesterol and triglycerides responded favorably to treatment. There was also a reduction in various inflammatory markers and products of oxidation, suggesting ALA treatment had potent antioxidant effects.

ALA may improve symptoms of diabetic neuropathy, as demonstrated by a controlled study of 12 patients with type 2 diabetes. Daily administration of 600 mg of ALA for three weeks improved numbness, pain, and burning in diabetic neuropathy. A recent study of 181 diabetes patients compared various doses of ALA with placebo. Daily doses of 600, 1,200, or 1,800 mg of all improved symptoms of diabetic neuropathy to approximately the same degree-- greater than 50% of patients responded in all three groups—the response was considerably less favorable in the placebo group (26%).

ALA reduced pain, increased muscle strength, and improve sensory function. Importantly, patients taking the 1,800 mg dose had increased nausea, vomiting, and dizziness. The results of this study suggest 600 mg of ALA per day is sufficient to achieve favorable outcomes in diabetic neuropathy without an increase in adverse events. These results have been verified in other studies.

**Grape seed extract** - Grape seed extract is a fat soluble component of grape seeds isolated into a pill or tablet form. Grape seed extract is not one molecule but rather large amounts of vitamin E and other antioxidants such as procyanidins, flavonoids, polyphenols (like resveratrol), and linoleic acid. When animals with diabetes are given grape seed extract, they have significantly reduced levels of potentially damaging oxidative molecules. In a double-blinded, crossover trial, 32 type 2 diabetes patients on conventional medical therapy received 600 mg per day of grape seed extract or placebo for four weeks. Grape seed extract significantly improved markers of oxidative stress, C reactive protein, and reduced glutathione compared to placebo. In a review of randomized controlled trials comprised of nearly 400 individual patients found grape seed extract significantly reduced diastolic blood pressure but had no apparent effect on cholesterol levels or C-reactive protein.

**Evening Primrose Oil** - Evening primrose oil is a natural product derived from the primrose plant and has been used by natural practitioners for a variety of ailments, from skin disorders to cancer to mental health conditions. Particularly strong data exists for the use of evening primrose oil in the treatment of breast pain and osteoporosis. One of the main components of evening primrose oil is gamma-linolenic acid. In 111 people with mild diabetic neuropathy, a daily, oral dose of 480 mg of gamma-linolenic acid significantly improved 13 parameters or symptoms associated with neuropathy including hot and cold sensitivity, muscle strength, and sensation. When evening primrose oil was given to diabetic rats, it blocked various hallmarks of diabetic neuropathy as seen by microscope/electron microscope.

**Bitter melon** - The fruit of Momordica charantia (a.k.a. Bitter Melon, Bitter Gourd, karera) has been used in traditional herbal medicine for the treatment of rheumatism, gout, dysmenorrhea, jaundice, and disorders of the liver and spleen. Administration of 230 g/day of karera him for 8-11 weeks to a group of nine patients with DM, significantly improved the results of oral glucose tolerance tests. In a 4-week, multicenter, randomized, double-blind trial, four groups of people with type 2 diabetes received bitter melon 500 mg/day, 1,000 mg/day, and 2,000 mg/day or metformin 1,000 mg/day. Patients receiving metformin and 2000 mg a day of bitter melon achieved significant reductions in a maker of diabetes status called fructosamine, while lower doses of bitter melon did not have a significant effect. In this systematic review performed in 2012 found for randomized clinical trials using Momordica charantia in the treatment of diabetes. Despite four clinical trials incorporating nearly 500 participants, the authors of this review concluded there was not enough evidence yet available to evaluate the effects of this natural substance on type 2 diabetes. Since the publication of that review, however, 4.8 g of Momordica charantia a day in powder form was able to decrease the incidence rate of metabolic syndrome in a group of 42 participants. While these results are promising, larger studies of Momordica charantia are likely required to determine their efficacy in treating type 2 diabetes.

**Fenugreek seeds** - Fenugreek (Trigonella foenum graecum) has been used in cooking and medicine for at least 3,500 years. Traditional uses have ranged from the treatment of indigestion and lack of appetite to ameliorating menopausal symptoms and labor induction in pregnant women. Research into fenugreek, particularly the seeds of the plant, has revealed the natural product may be able to reduce blood sugar levels. There have been at least 10 clinical trials over the past 25 years that have examined the ability of fenugreek preparations to affect important indices in type 2 diabetes such as fasting blood glucose, glucose tolerance, hemoglobin A1C, and the amount of insulin in the blood after fasting. Fenugreek has taken various forms in these trials including powdered fenugreek seeds, a water based extract of seeds, and fenugreek baked into unleavened bread called chapati. The daily dose of fenugreek seed varied from 1 to 100 g per day. Across clinical trials, fenugreek significantly reduced fasting blood glucose and glucose tolerance and was able to hemoglobin A1 C by almost a full percentage point. Based on this analysis, the authors recommend a dose of fenugreek of at least 5 g per day though they acknowledge larger, well-controlled studies are needed.

**Burdoc** - The roots, leaves, and seeds of the burdock plant (Arctium lappa) have been used for a variety of medicinal purposes. Preparations of burdock are available for oral use and topicaly, for skin conditions. In an uncontrolled study, burdock root in doses of 54-81 g/day reduced insulin requirements in people with diabetes. The effect disappeared when the treatment was discontinued and resumed once Burdock root was restarted. Fructus Arctii, the name given to the fruit of the burdock plant in Traditional Chinese Medicine, reduced blood glucose, triglycerides and total cholesterol in rodents with diabetes.

**Gymnema** - Gymnema (Gymnema sylvestre) is a leafy plant common in India and North Africa and has been used in Ayurvedic medicine to treat diabetes. When the leaves of Gymnema are chewed, users report the suppression of “sweet” taste buds. When extracts of the plant are placed in a laboratory dish with insulin secreting pancreatic cells, the extract stimulates insulin release. When a group of 27 individuals with type 1 diabetes were given 400 mg per day of Gymnema, they experienced a decrease in the amount of insulin they needed for glycemic control along with a drop in fasting blood glucose and hemoglobin A1C. The water-soluble extract of Gymnema sylvestre also appears to work in type 2 diabetes patients. Researchers from the same group gave the extract to 22 people with type 2 diabetes who were also taking sulfonylureas. The same dose administered for 18 to 20 months significantly reduced blood glucose and hemoglobin A1C and allowed patients to reduce the amount of sulfonylurea they were taking.
tolerance test in both type 2 diabetes patients and healthy have focused on American ginseng. Doses from 1 to 9 g of in rats.

Cinnamon - Cinnamon (Cinnamomum zeylanicum) is a familiar name and is in virtually every kitchen in America. However, the cinnamon found in most US homes is a less expensive form of cinnamon called cassia (Cinnamomum cassia) and is derived from a different plant than “true cinnamon” which is the Cinnamomum zeylanicum. True cinnamon may also be called Ceylon cinnamon. More than 300 species of cinnamon belong to the Lauraceae family. Clinical studies on cinnamon may include either form, so it is sometimes difficult to determine doses and potencies. Some researchers believe the active component in cinnamon and the reason it can lower blood glucose levels is a compound called cinnamaldehyde. Cinnamaldehyde dose-dependently improved glycemic control in diabetic animals. Cinnamon may help increase insulin levels in the blood and increase the amount of glucose stored in the liver as glycogen. Cinnamon may also mimic the effect of insulin itself.

Researchers compiled a meta-analysis of ten randomized clinical trials examined the effect of cinnamon on blood glucose levels and diabetic endpoints. Seven trials used the cassia form of cinnamon in capsule or powder form. Doses ranged from 120 mg to 6 g per day. Three of the 10 trials found cinnamon significantly reduced hemoglobin A1C levels though when combined across all 10 trials, the effect was no longer statistically significant. On the other hand, most trials found a significant reduction in fasting blood glucose with cinnamon consumption. The average reduction was approximately 25 mg/dL—a substantial decrease. Cinnamon use was associated with significant reductions in LDL and total cholesterol and triglycerides across the 10 studies. No serious adverse events were reported in any of the clinical trials.

American Ginseng and Panax Ginseng - American ginseng (Panax quinquefolium) and the natural product known simply as ginseng (Panax Ginseng) are distinct plants but both may have beneficial effects in diabetes. Both contain substances that can lower blood glucose levels. Recent clinical trials have focused on American ginseng. Doses from 1 to 9 g of ginseng were equally able to improve results on in oral glucose tolerance test in both type 2 diabetes patients and healthy controls. Interestingly, the response of blood glucose reduction in healthy people only occurred if the ginseng was given at least 40 minutes before the glucose tolerance test. Ginseng supplementation (1 g per day) over eight weeks in people with type 2 diabetes significantly reduced fasting blood glucose and hemoglobin A1C values compared to those who took placebo. A subsequent trial among overweight or obese individuals with either impaired glucose tolerance or newly diagnosed type 2 diabetes found 30 days of treatment with a ginseng root extract totaling 8 g per day failed to influence in insulin-secreting cells in the pancreas or insulin sensitivity. The authors note the preparations of ginseng they used in this study may not have been effectively absorbed and could explain the lack of effect. They also described the fact significant weight loss occurred in people who consumed ginseng and the weight loss may have been responsible for the improvement in diabetes. Adverse effects that have been associated with ginseng are insomnia, diarrhea, vaginal bleeding, breast pain, headache, and the Stevens-Johnson syndrome.

Mulberry - There are over 150 named species of mulberry, each of the genus Morus. The most often studied species are Morus alba (white mulberry) and the closely related Morus indica. Both the leaves and berries of the mulberry plant have been tested in various laboratory and animal studies and found to have properties that would potentially make them useful in people with diabetes (e.g., the ability to lower glucose, antioxidants effects). For example, Morus alba leaf extracts decreased the amount of food consumed by diabetic rats and also decreased blood sugar levels. Likewise, daily administration of 1 g per kilogram body weight of mulberry leaf decreased hemoglobin A1C in diabetic rats by over two percentage points (un-treated: 9.02 +/- 0.30%; treated: 7.68 +/- 0.30%) along with reductions in blood glucose and oxidative products. An extract obtained from mulberry fruit, on the other hand, reduced fasting blood glucose to nearly the same degree as metformin (200 mg per kilogram of mulberry fruit extract vs. 300 mg per kilogram of metformin).

A study of 24 people with type 2 diabetes showed that a compound derived from mulberry leaves had significant improvement in blood sugar control compared to a group that received glibenclamide, a commonly used anti-diabetes drug. A form of mulberry powder that was specifically manufactured to contain high amounts of a particular molecule, mulberry 1-deoxynojirimycin (DNJ), was able to keep blood glucose levels low after healthy volunteers consumed 50 g of table sugar. Incidentally, the researchers found the highest amount of DNJ was contained in young mulberry leaves taken from the top part of the branches during summer. A similar effect was observed in patients with type 2 diabetes when they were given 75 g of table sugar along with 1 g of a mulberry extract simultaneously. The mulberry extract apparently blunted the sugar-induced rise in blood glucose in both healthy volunteers and diabetic patients.

Aloe - Aloe (Aloe barbadensis) is a succulent and part of the Liliaceae family of plants. While the use of external aloe as a soothing agent is well known, the plant is also used as an oral treatment. Aloe has been used to treat various non-skin illnesses for some time. A group of pharmacists recently reviewed the effects of aloe in the treatment of diabetes and found seven relevant clinical trials. Five out of seven clinical studies in humans that examined relevant features of diabetes found oral aloe vera taken by people with diabetes or insulin insensitivity was able to significantly lower fasting blood glucose levels. The other two studies found a reduction was not statistically significant. Of the studies that measured hemoglobin A1C, aloe reduced this measure significantly—by over 20% in one study. Oral aloe vera consistently reduced triglyceride levels.

References


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