LITERATURE REVIEW
Literature Review

Although diabetes has been recognized since antiquity and treatments were known since the middle ages, but the elucidation of pathogenesis occurred mainly in the 20th century [28]. Two European researchers Joseph Von Mering and Osker Minkowski in 1889 discovered the role of pancreas in diabetes. In 1921, Sir Frederick Grant Banting and Charles Herbert Best clarified the endocrine role of pancreas in insulin metabolism. They isolate the hormone insulin from bovine pancreas at the university of Toronto in Canada. This led to the availability of an effective treatment – insulin injections and the first clinical patient was treated in 1922. For this, Bating et al received the noble prize in Physiology or Medicine in 1923. The distinction between type-I and Type-II diabetes was made by Sir Harold Percival (Harry) Himsworth in 1935; he published his findings in January 1936 in the Lancet [29].

Diabetes is a chronic condition, marked by high levels of glucose in the blood. It is caused by deficient production of the hormone insulin, or resistance to its action. Diabetes is a serious condition that raising a person’s risk for heart and cardiovascular disease. There are four main types of diabetes mellitus:

**A-Type I Diabetes (DM1)** - formerly known as Juvenile Onset Diabetes, Insulin-Dependant Diabetes or childhood diabetes (IDDM). Insulin-dependant diabetes mellitus is caused by damage to the pancreas. With Type I diabetes, the deficiency of insulin is due to a decline in the number of beta cells the pancreas contains. In most people with Type I diabetes, the immune system makes a mistake, attacking the beta cells and causing them to die. Glucose then builds up in the blood and causes diabetes. Patients with type 1 diabetes need to take insulin. Dietary control in type 1 diabetes is very important and focuses on balancing food intake with insulin intake and energy expenditure from physical exertion.

In type 1 diabetes, the disease process is more severe than with type 2, and onset usually begins in childhood:

- Beta cells in the pancreas that produce insulin are gradually destroy Eventually insulin deficiency is absolute.
Without insulin to move glucose into cells, blood glucose level becomes excessively high, a condition known as hyperglycemia.

Because the body cannot utilize the sugar, it spills over into the urine and is lost.

Weakness, weight loss, and excessive hunger and thirst are among the consequences of this "starvation in the midst of plenty."

Type I diabetes exhibits the following warning signs:

- Losing weight without trying
- An increased need to urinate
- Increased hunger
- Increased thirst
- Trouble seeing
- Feeling tired and/or
- Going into a coma

For Type I diabetics, treatment usually consists of a healthy diet, exercise, and insulin shots to replace the insulin that your body no longer produces. This is necessary to keep their blood glucose within certain limits.

**B-Type II Diabetes (DM2) - formerly known as Adult Onset Diabetes, Non-Insulin-Dependent Diabetes (NIDDM).** Type II diabetes produces mild symptoms, and can be controlled with a healthy diet, exercise and weight loss. In some cases, weight loss, diet and exercise are not enough to control the glucose level.

Type 2 diabetes is the most common form of diabetes, with about 95% of diabetes falling into the Type II category. About 20 million Americans have type 2 diabetes, and half are unaware they have it. With Type II diabetes, glucose builds up in the blood – not because not enough insulin is present, but probably because cells lose their insulin receptors and become less sensitive to insulin. Type II diabetes usually (though not always) occurs in individuals who are over 40 years of age who are overweight. The disease mechanisms in type 2 diabetes are not wholly known, but some experts suggest that the disease may involve the following three stages in most patients:
• The first stage in type 2 diabetes is the condition called *insulin resistance*. Although insulin can attach normally to receptors on liver and muscle cells, certain mechanisms prevent insulin from moving glucose (blood sugar) into these cells where it can be used. Most patients with type 2 diabetes produce variable, even normal or high, amounts of insulin, and in the beginning this amount is usually sufficient to overcome such resistance. Patients whose blood glucose level is higher than normal, but not yet high enough to be classified as diabetes, are considered to have "pre-diabetes." It is very important that people with pre-diabetes control their weight to stop or delay the progression to diabetes.

• Over time, the pancreas becomes unable to produce enough insulin to overcome resistance. In type 2 diabetes, the initial effect of this stage is usually an abnormal rise in blood sugar right after a meal (called *postprandial hyperglycemia*). This effect is now believed to be particularly damaging to the body.

• Eventually, the cycle of elevated glucose further impairs and possibly destroys beta cells, thereby stopping insulin production completely and causing full-blown diabetes. This is made evident by *fasting hyperglycemia*, in which elevated glucose levels are present most of the time.

**Risks for Diabetes**

- Individuals with parents or siblings with diabetes
- People over the age of 45
- People who are overweight
- People who do not exercise regularly
- People with low HDL cholesterol or high triglycerides
- Women who had gestational diabetes or who had a baby weighing 9 pounds or more at birth.

**C) Gestational diabetes mellitus or pregnancy-induced diabetes:** Gestational diabetes can occur during pregnancy and increases the risk of developing diabetes later in life.
D) **Secondary diabetes mellitus:** it is caused by genetic conditions, pancreatic diseases (e.g. inflammation, surgery or malignancy of the pancreas, etc.), drugs (e.g. steroids like prednisolone, pentamidine, excess thyroid hormone, etc.) or other medical conditions (acromegaly, Cushing syndrome, pheochromocytoma, hyperthyroidism, congenital rubella, etc). Medications such as thiazide diuretics or oral contraceptives can precipitate diabetes in a person predisposed to get it later. Symptoms depend on the type and duration of diabetes. Some of the signs and symptoms are related to the high blood sugar levels. These include:

- Increased urination,
- Increased thirst and
- Hunger.

Other common symptoms:

- Fatigue,
- Blurred vision,
- Urinary and vaginal infections
- Skin infections, especially fungal or more serious bacterial infections.
- Frequently upset stomach, stomach pains, nausea and vomiting

There may be weight loss, especially if the amount of insulin made by the body is decreasing. The person can become drowsy and then go into coma. This is called **Ketoacidosis**, and usually occurs in DM-1. Rarely, if the diabetes is completely out of control, it can also occur in DM-2. Other symptoms of ketoacidosis include:

- Deep rapid breathing, sometimes with a fruity odour to the breath
- Pain in the stomach, with nausea and vomiting.

Diabetes affects all organs of the body. The long-term effects include:

1. **Retinopathy:** damage to the retina of the eye that can cause blindness.
2. **Nephropathy:** damage to the kidneys that can lead to kidney failure.
3. **Peripheral neuropathy**: damage to the nerves in the limbs, which causes numbness, tingling (e.g., feeling like crawling of ants over the skin) and pain in the feet, legs and hands.

4. **Autonomic neuropathy**: damage to the nerves of the internal organs, resulting in problems with digestion, diarrhoea, impotence, fast heartbeat ("tachycardia") and altered blood pressure.

5. **Atherosclerosis**: hardening or blockage of arteries, which can lead to heart attack and stroke ("Brain attack").

6. **Peripheral vascular disease**: damage to the arteries causes poor circulation in the legs and feet. This poor circulation, along with nerve damage, can result in serious foot and leg infections that may require amputation.

7. **Skin infections**, especially fungal infections such as ringworm, jock itch, and athlete's foot. Other bacterial infections are also common and can occasionally be life threatening.

8. **Vaginal infections**, as high levels of sugar encourage the growth of yeast.

9. **Urinary tract infections**.

Heart disease is the leading cause of death in America today, killing an estimated one in every three Americans. Several factors, such as high blood cholesterol levels, hypertension, cigarette smoking, and diabetes, are chief culprits in the promotion of heart disease.

Ischemia (is-KE'me-ah) is a condition in which the blood flow (and thus oxygen) is restricted to a part of the body. It is an episodic disease resulting in a temporary stoppage of blood in the coronary arteries and ischaemia of the heart muscle. Ischemia means that the amount of oxygen supplied to the tissue is inadequate to supply the needs of the tissue. When the myocardium becomes ischemic, it does not function optimally. When large areas of the myocardium becomes ischemic, there can be impairment in the relaxation and contraction of the myocardium.

**Symptoms of Ischaemic Heart Disease**

- Sensation of feeling the heart beat (palpitations)
- Shortness of breath, especially with activity
- Shortness of breath that occurs after lying down for a while
• Fatigue, weakness, faintness
• Chest pain
• Orthopnoea
• Slurred or garbled speech or difficulty understanding others
• Dizziness, loss of balance or loss of coordination
• Lack of coordination
• Falling (caused by weakness in the legs)
• Cough
• Decreased alertness or concentration

Causes of Ischaemic Heart Disease

• Ischemic cardiomyopathy is a common cause of congestive heart failure.
• Ischemic cardiomyopathy results when the arteries that bring blood and oxygen to the heart are blocked.
• But in contrast to a stroke, which involves a more prolonged lack of blood supply and causes some permanent damage to your brain tissue, a TIA doesn't leave lasting effects to your brain.
• Blood clot traveling to the brain from somewhere else in the body (e.g., heart)
• Patients with this condition may at one time have had a heart attack, angina, or unstable angina.
• Injury to blood vessels
• Underlying medical conditions are other medical conditions that may possibly cause Ischemic heart disease.

Treatment of Ischaemic Heart Disease

Here is the list of the methods for treating Ischaemic Heart Disease:

• These treatments can improve blood flow to the damaged or weakened heart muscle.
• If you smoke or drink alcohol excessively, stop doing so, because these habits increase the stress on the heart.
• Patients with this disorder usually will have a cardiac catheterization performed to see if they are candidates for bypass surgery or angioplasty ("balloon procedure").
• A heart transplant may be recommended for patients who have failed all the standard treatments and still have very severe symptoms.
• These medications make your platelets, one of the circulating blood cell types, less likely to stick together.
• Depending on a patient's medical history and the results of a medical examination, the doctor may recommend drug therapy or surgery to reduce the risk of stroke in people who have had a TIA.
• Aspirin is the most commonly used medication; others include dipyridamole, clopidogrel, Aggrenox or heparin, coumadin, or other similar medications.
• Surgery (carotid endarterectomy, removal of atherosclerotic plaque from the carotid arteries in the neck) may be appropriate for some people, particularly those with carotid artery stenosis of greater than 70% of the artery and without coexisting terminal disease or dementia.

Risk Factors and Coronary Heart Disease

• **Increasing age** — Over 83 percent of people who die of coronary heart disease are 65 or older. At older ages, women who have heart attacks are more likely than men are to die from them within a few weeks.
• **Male sex (gender)** — Men have a greater risk of heart attack than women do, and they have attacks earlier in life. Even after menopause, when women's death rate from heart disease increases, it's not as great as men's.
• **Heredity (including Race)** — Children of parents with heart disease are more likely to develop it themselves. African Americans have more severe high blood pressure than Caucasians and a higher risk of heart disease. Heart disease risk is also higher among Mexican Americans, American Indians, native Hawaiians and some Asian Americans. This is partly due to higher rates of obesity and diabetes. Most people with a strong family history of heart disease have one or more other risk factors. Just as you can't control your age, sex and race, you can't control your
family history. Therefore, it's even more important to treat and control any other risk factors you have.

- **Tobacco smoke** — Smokers' risk of developing coronary heart disease is 2–4 times that of nonsmokers. Cigarette smoking is a powerful independent risk factor for sudden cardiac death in patients with coronary heart disease; smokers have about twice the risk of nonsmokers. Cigarette smoking also acts with other risk factors to greatly increase the risk for coronary heart disease. People who smoke cigars or pipes seem to have a higher risk of death from coronary heart disease (and possibly stroke) but their risk isn't as great as cigarette smokers'. Exposure to other people's smoke increases the risk of heart disease even for nonsmokers.

- **High blood cholesterol** — As blood cholesterol rises, so does risk of coronary heart disease. When other risk factors (such as high blood pressure and tobacco smoke) are present, this risk increases even more. A person's cholesterol level is also affected by age, sex, heredity and diet.

- **High blood pressure** — High blood pressure increases the heart's workload, causing the heart to thicken and become stiffer. It also increases your risk of stroke, heart attack, kidney failure and congestive heart failure. When high blood pressure exists with obesity, smoking, high blood cholesterol levels or diabetes, the risk of heart attack or stroke increases several times.

- **Physical inactivity** — An inactive lifestyle is a risk factor for coronary heart disease. Regular, moderate-to-vigorous physical activity helps prevent heart and blood vessel disease. The more vigorous the activity, the greater your benefits. However, even moderate-intensity activities help if done regularly and long term. Physical activity can help control blood cholesterol, diabetes and obesity, as well as help lower blood pressure in some people.

- **Obesity and overweight** — People who have excess body fat — especially if a lot of it is at the waist — are more likely to develop heart disease and stroke even if they have no other risk factors. Excess weight increases the heart's work. It also raises blood pressure and blood cholesterol and triglyceride levels, and lowers
HDL ("good") cholesterol levels. It can also make diabetes more likely to develop. Many obese and overweight people may have difficulty losing weight. But by losing even as few as 10 pounds, you can lower your heart disease risk.

- **Diabetes mellitus** — Diabetes seriously increases your risk of developing cardiovascular disease. Even when glucose (blood sugar) levels are under control, diabetes increases the risk of heart disease and stroke, but the risks are even greater if blood sugar is not well controlled. About three-quarters of people with diabetes die of some form of heart or blood vessel disease. If you have diabetes, it's extremely important to work with your healthcare provider to manage it and control any other risk factors you can.

Recently experimental findings suggests that over production of ROS, lowered antioxidant defense and alteration of enzymatic pathways with poorly controlled DM, which can contribute to metabolic and pathological complications along with depletion of natural antioxidants. (30,31). McCord and Fridovich opened the field of free radicals and oxidative stress when they discovered an enzyme superoxide dismutase (SOD) (32). Since then reactive oxygen species (ROS) has come to occupy an amazingly central role in a wide variety of diseases. Overall, free radicals have been implicated in the development of at least 50 diseases -includes DM & IHD are two of the most widespread diseases associated with free radical damage.

**Free Radical “Causes of Degenerative Disease”**

Free radicals are formed naturally in the body - for example, as byproducts of normal metabolism, by the breakdown of bacteria by white blood cells, or by enzymatic reactions; they are also formed, in ever-increasing numbers, outside the body by pollution, radiation, cigarette smoke, motor vehicle emissions, and many other processes. These environmental free radicals then enter the body through the skin, respiration, and other means. Even oxygen, which we need in order to survive, can initiate a free-radical chain reaction in our bodies.

A free radical is a molecular fragment with an unpaired electron in its outer orbital ring, causing it to be highly oxidative, unstable, and to react instantaneously with
other substances.(33,34) Within a few millionths of a second, free radicals have the potential to react with and damage nearby molecules and cell membranes. Such reactions can then produce an explosive cascade of free radicals in a multiplying effect--a literal chain-reaction of damage (35-40). Ongoing free radical reactions in normal cellular metabolism occur continuously in all cells of the body and are necessary for health.(35-37, 41-50). The highly reactive free radicals continuously produced within healthy human cells include hydroxyl radicals, superoxide radicals, and excited or singlet-state oxygen radicals. They are commonly referred to collectively as "free oxygen radicals," or often as simply "free radicals"(37,41-46, 51). Each uncontrolled free radical has the potential to multiply by up to a million-fold in a chain reaction, much like a nuclear reaction. (33,35-37,52-54). When free radicals react in the body they in turn produce other highly reactive molecules, including hydrogen peroxide, lipid peroxide, and other peroxides. Peroxides are metastable, highly reactive, corrosive molecules and also react rapidly, producing additional organic radicals in surrounding tissues. (33, 34). In a similar way, free oxygen radicals in cells produce damaging lipid peroxides, oxyarachidonate and oxycholesterol products (35, 52, 53, 55, 56).

There is considerable evidence from invitro and invivo studies that in a variety of tissues, hyperglycemia and elevated free fatty acids (FFA) level, both alone and in combination may results in the generation of highly reactive oxygen species (ROS) consequently increase oxidative stress in DM & IHD. It is implicated that four major pathways of glucose metabolism, which includes- increased polyol pathway, non-enzymatic glycation of proteins and glucose autoxidation can increase the production of free radicals.

In non-enzymatic glycation glucose undergoes a nucleophilic addition reaction with proteins to form the schiff base and subsequently undergoes an Amadori compound. The Amadori compound have been implicated in the formation of H$_2$O$_2$ in vitro via 2 pathways (57). One pathway is the 1,2 -enolization pathway, which under anaerobic conditions lead to the formation of 3-deoxyglucosone. The 3-deoxyglucosone is a major and highly reactive intermediate in the non-enzymatic glycolysation and a potent cross linker responsible for the polymerization of proteins to AGEs. In the presence of a suitable electron acceptor, however, enolization would occur to form H$_2$O$_2$ and glucosone.
The other pathway is 2,3-enolization pathway, which leads to 1-deoxyglucosone and the putative 1,4-deoxyglucosone (57). Under oxidative conditions, however, the 2,3-enediol is thought to generate \( \text{H}_2\text{O}_2 \) and carboxymethyllysine (57). AGEs accumulate on long-lived macromolecules which results in abnormalities of cell, tissue function (58) and contribute to increase vascular permeability in both micro & macro-vascular structures by binding to a specific macrophage receptor (57). This process induced the synthesis and secretion of cytokines such as tumor necrosis factor (TNF) & IF-1 which causes endothelial dysfunction.

In glucose-autoxidation reaction, monosaccharides and fructose lysine can reduce molecular oxygen (58) and the resulting products formed are superoxide, hydroxyl radical and hydrogen peroxide. FR also accelerates the formation of advanced glycosylation end-products, which in turn further generate more FR [59]. FR can also be generated by polyol pathway (60). Aldose reductase catalyzing the reduction of glucose by NADPH to sorbitol which can, in turn, be oxidated to fructose by sorbitol dehydrogenase (SDH) leading to redox imbalance (NAD⁻/NADH ratio). An increase in NAD⁻/NADH ratio is linked to could be another source of increased oxidative stress and down regulation of antioxidative system via the reduction of PGG₂ to PGH₂ by prostaglandin hydroperoxidase.

Oxidative stress during ischemia and especially upon reperfusion results from the excessive generation of radicals and the deficiency of protection by enzymes and scavengers (61,62). These sources include enzymes, such as xanthine Oxidase, cytochrome oxidase, and cyclooxygenase, and the oxidation of catecholamines. During ischemia xanthine dehydrogenase is converted, probably by an increase of cytosolic calcium (63), by limited proteolysis, or by the oxidation of thiol groups to the oxidase form (64-66). At the same time, ATP is degraded to hypoxanthine, which accumulates in ischemic tissue (67). The ischemia and reperfusion induced calcium overload would activate phospholipases [68, 69] that in turn may degrade cell membrane phospholipids, releasing arachidonic acid. Studies with isolated myocytes [70] have shown that lipid peroxidation can be activated by increasing calcium concentration.

Finally, the autooxidation of catecholamines, which are abundantly released from the ischemic myocardium, could provide through the formation of adrenochrome oxygen
free radicals (71, 72). Radicals attack proteins and cause lipid peroxidation, resulting in block of most K+ channels, activation of the SR Ca+ release channel, and eventually the mitochondrial megachannel. Free radical damage to the calcium-magnesium pump allows excessive calcium to diffuse into the cell. If the pump cannot prevent calcium from leaking into cells, and keep magnesium from leaking out, the cell becomes poisoned and soon dies. Neutrophils represent a major source of free radicals during ischemia and reperfusion. In infarcted myocardium, after 24 h, the neutrophil content is increased by 17-fold. (73).

Protection Against Oxygen Free Radicals

Oxidative stress is the condition in which a lack of balance exists between the oxidant stimuli and the various antioxidants. Oxidative stress is associated with several cardiovascular diseases, including atherosclerosis, hypertension, heart failure, stroke, and diabetes. (74-76). Oxidation of low density lipoprotein (LDL) appears to play a key role in the pathogenesis of atherosclerosis (77). Oxidative stress also plays a key role in endothelial dysfunction associated with these diseases, as superoxide (O$_2^-$) inactivates nitric oxide (NO) and thereby produces endothelial dysfunction (78,79). Because endothelial dysfunction is associated with, and may contribute to, an increased risk of cardiovascular events (80,81), oxidative stress may be causally related to, as well as associated with, cardiovascular events.

Antioxidants are highly diverse in source, effect, and use. Antioxidants protect against damage from free radicals by preventing the formation of excess free radicals; scavenging free radicals after they are formed and before they damage other molecules, & repairing or replacing damaged molecules. Technically, they are substances that prevent or inhibit oxidation, and they can be found in hundreds of naturally occurring substances and forms, which in turn mitigates the risk of developing chronic diseases.

Scientists are discovering that there is a tighter link between diet and health-antioxidant properties are a strikingly common feature in phytochemicals; they therefore play an important role in inhibiting aging processes related to oxidative damage caused by free radicals. In the last years there has been a constantly rising interest in the
antioxidative constituents of various medicinal plants, due to their potential in controlling the levels of free radicals and the process of lipid peroxidation (82, 83).

Many early theories speculated that antioxidants protect against cancer mainly by preventing the formation and scavenging of free radicals. Oxidative stress caused by free radical damage to DNA and other molecules in the body is thought to be a factor in the development of every major chronic disease, including cancer, atherosclerosis and heart disease. Research (84) during the past decade shows that some antioxidants may exert their protective effects mainly by repairing and replacing free radical damaged structures, or inducing enzymes to remove carcinogens before they cause damage.

It is already established that chromium supplement in certain required amount in (late-onset) diabetes significantly improve insulin activity and blood glucose levels. But while cinnamon and other herbs and spices contain small amounts of chromium (85), researchers remained unconvinced that this is related to their antidiabetic activity. In fact, most of the chromium found in herbs and spices is a result of contamination from harvesting and processing, and is not in a biologically active form.

In 2000, the puzzle was finally solved when Walter Schmidt in the Agricultural Research Service NMR laboratory at Beltsville, MD, identified methyl hydroxychalcone polymer (MHCP) as the most active compound responsible for this antidiabetic activity of cinnamon. MHCP increases glucose metabolism roughly 20-fold in a test tube assay of fat cells. Research in 1998 by Donald Grave at Iowa State University suggests that the cinnamon components act like insulin to affect protein phosphorylation-dephosphorylation reactions in the intact fat cell (86).

Cinnamon has been used for several thousand years in traditional Ayurvedic and Greco-European medical systems. Cinnamomum zeylanicum is an evergreen tropical tree, belonging to the Lauraceae family. Cinnamon barks and leaves are widely used as spice and flavoring agent in foods and for various applications in medicine (87).

Native to tropical southern India and Sri Lanka, the bark of this evergreen tree is used to manage conditions such as nausea, bloating, flatulence, and anorexia.
"Cinnamon is mentioned in one of the earliest books on Chinese botanical medicine, dated 2,700 B.C. It was so highly treasured that it was considered more precious than gold. The history of the trade of cinnamon, from China to Indonesia, Africa, Rome, Egypt and Greece via sea route is a fascinating topic in economics, religion, politics and medicine. This is the history of the “cultures of the world.”

Main Constituents:

The essential oil of cinnamon bark (max. 4%) is dominated by the two phenylpropanoids cinnamaldehyde (3-phenyl-acrolein, 65%-75%) and eugenol [4-(1-propene-3-yl)-2-methoxy-phenol, 5%-10%]. Other phenylpropanoids (safrole, coumarin [0.6%] cinnamic acid esters), mono- and sesquiterpenes, although occurring only in traces, do significantly influence the taste of cinnamon. Another trace component relevant for the quality is 2-heptanone (methyl-n-amyl-ketone). From cinnamon leaves, another essential oil (1%) can be obtained, consisting mainly of eugenol (70%-95%) and can be used as a substitute for clove. Small amounts (1%-5%) of cinnamaldehyde, benzyl benzoate, linalol and B-caryophyllene also have been found. A completely different composition is found in the essential oil of cinnamon root bark; in this case, camphor (60%) dominates. This oil is not used commercially. In cinnamon fruits ("cassia buds," "cinnamon buds"), the main components are trans-cinnamyl acetate and B-caryophyllene (88 to 90).

Health Benefits:

1. Fights tooth decay: "Cinnamon is an antiseptic that helps kill the bacteria that cause tooth decay and gum disease" - Daniel B. Mowrey, PhD, author of The Scientific Validation of Herbal Medicine (91,92).

2. Clears up urinary-tract infections: One German study showed that cinnamon "suppresses completely" the cause of most urinary-tract infections (Escherichia coli bacteria) (91,92).

3. Allows diabetics to use less insulin: Some studies have shown that cinnamon helps people with diabetes metabolize sugar better. Researchers discovered that cinnamon
reduces the amount of insulin necessary for glucose metabolism in patients with type-II diabetes. "One-eighth of a teaspoon of cinnamon triples insulin efficiency," according to James A. Duke, PhD, a botanist retired from the U.S. Department of Agriculture and author of *The CRC Handbook of Medicinal Herbs*. Dr. Duke suggests people with adult-onset diabetes discuss cinnamon's benefits with their doctor. Taking 1/2 to 3/4 teaspoon of cinnamon with each meal may help control blood sugar levels. Cinnamon might not only stimulate insulin receptors, but also inhibit an enzyme that inactivates them, thus significantly increasing cells' ability to use glucose (91,92,93).

4. **Antioxidant capacity:** Cinnamon is a powerful antioxidant that when compared to six other antioxidant spices anise, ginger, licorice, mint, nutmeg and vanilla and the chemical food preservatives BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene), and propyl gallate, it prevented oxidation more effectively (94,95).

5. **Also helps cholesterol:** cinnamon has shown promise in enhancing insulin's action remove artery-damaging free radicals from the blood and improve function of small blood vessels by lowering cholesterol. Onions, garlic, Korean ginseng, and flaxseed have the same effect (93, 94).

6. **A good source of calcium and fiber:** Cinnamon is an excellent source of the trace mineral manganese and a very good source of dietary fiber, iron and calcium. The fiber in cinnamon also might provide relief from constipation or diarrhea (91).

7. **Anti-clotting actions:** The cinnaldehyde in cinnamon helps prevent unwanted clumping of blood platelets by inhibiting the release of an inflammatory fatty acid called arachidonic from platelet membranes and reducing the formation of an inflammatory messaging molecule called thromboxane A2 (96).

8. **Antimicrobial activity:** Eugenol and cinnamaldehyde are two very important terpenoids found in cinnamon. Cinnamaldehyde and cinnamon oil vapors act as potent antifungal agents. In a study published in the August 2003 issue of the *International Journal of Food Microbiology*, the addition of a few drops of cinnamon essential oil to 100 ml (approximately 3 ounces), inhibited the growth of the foodborne pathogenic
Bacillus cereus for at least 60 days. A Japanese animal study revealed that cinnamon also might help prevent ulcers (96, 97).

9. **Cinnamon's scent boosts brain function:** Research by Dr. P. Zoladz, presented April 24, 2004, at the annual meeting of the Association for Chemoreception Sciences in Sarasota, Fla., found chewing cinnamon-flavored gum or smelling cinnamon enhanced study participants' cognitive processing. Cinnamon improved participants' scores on tasks related to attentional processes, virtual recognition memory, working memory and visual-motor speed while working on a computer-based program (98).

10. **Fighting allergies:** The diterpenes found in cinnamon oil have shown antiallergenic activity.

11. **Miscellaneous:** Cinnamon makes a nice nontoxic bug repellent when sprinkled in the kitchen cabinets (in large amounts it even keeps away fire ants as long as it is freshly applied around their mounds). A half teaspoon of cinnamon each day can reduce your stroke risk with these effects:

- Reduce blood sugar levels in non-insulin dependent diabetics and normalize blood sugar levels in non-diabetics
- Lower LDL-cholesterol and triglyceride levels
- Prevent blood clots
- Lower high blood pressure
- Promote weight loss and maintenance
- Lower the risk for heart disease

The essential oil from C. zeylanicum barks is rich in trans-cinnamaldehyde with antimicrobial effects against animal and plant pathogens, food poisoning and spoilage bacteria and fungi (99-101). It has been established that the oils and extracts from cinnamon possess a distinct antioxidant activity, which is especially attributed to the presence of phenolic and polyphenolic substances [102-110]. In addition to traditional use, modern research has demonstrated a number of benefits resulting from cinnamon supplementation. These include improvements in blood sugar for Type-2 diabetics, improvements in body composition (e.g., increased lean mass), improvements in
cardiovascular parameters, and substantial antioxidant properties. One of the recent studies involved subjects with Type-2 diabetes who took 1 g/d, 3 g/d or 6 g/d of cinnamon extract (as Cinnulin PF®, from Integrity Nutraceuticals), researchers found 40 days of supplementation lowered fasting blood sugar by 18 to 29 percent [93]. The highest dose produced the most rapid response; however, the lowest dose produced the most sustained response over the course of the study. In addition, supplementation for 60 days caused significant drops in triglycerides (23 to 30 percent), low-density lipoprotein (LDL) cholesterol (7 to 27 percent) and total cholesterol (12 percent to 26 percent).

A more recent placebo-controlled, double blind study was conducted on 79 patients with Type 2 diabetes mellitus (112) Subjects were given 336 mg/d of a water-soluble cinnamon extract (as Cinnulin PF), corresponding to 3 g of cinnamon powder, or a placebo for four months. Those using the cinnamon experienced a significant 10.3 percent reduction in fasting blood sugar, compared to a non-significant 3.4 percent reduction in the placebo group. Studies in non-diabetics have also proven promising. In a placebo-controlled, double blind study involving 21 adults with metabolic syndrome (i.e., prediabetes), researchers administered 500 mg/d water-soluble cinnamon extract, or placebo for 12 weeks (113). Among those given the cinnamon extract, 83 percent experienced a significant decrease (about 8 percent) in fasting blood sugar; only 33 percent in the placebo group experienced a decrease.

The subjects taking the cinnamon extract also experienced a significant alteration in body composition, with body fat decreasing by 0.7 percent and muscle mass increasing by 1.1 percent, with no alterations in the subjects’ diet or physical activity. In addition, the researchers reported subjects taking cinnamon had a 3.8 percent reduction in systolic blood pressure. This finding is similar to that from a previous animal study in spontaneously hypertensive rats [114]. Cinnamon’s polyphenols are potent antioxidants, which could help to reduce oxidative damage caused by free radicals (115). One unpublished study, supported by Integrity Nutraceuticals, provided 21 obese, prediabetic subjects with Cinnulin PF or placebo and assessed antioxidant status and oxidative damage. Those who received the cinnamon experienced a 14-percent reduction in markers of oxidative damage, as well as an increase in markers of total antioxidant capacity.
The American Herbal Products Association’s (AHPA) *Botanical Safety Handbook* considers cinnamon to be safe for oral supplementation when used appropriately. 9 gm Cinnamon is GRAS (generally recognized as safe); however, AHPA suggests pregnant women not to exceed dosages commonly found in foods.