A New Approach to Diabetes

Diabetes: Starvation Amidst Plenty
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Sugar and Aging
R+ Made Better
I Want to Know...Q&A
Diabetes; Starvation Amidst Plenty
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Q & A

Cover Picture:
Scale representation of the typical North American’s lifelong sugar consumption.

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Starvation Amidst Plenty

Diabetes is said to be the disease of the century. The number of individuals suffering from diabetes in the year 2025 will be more than 10 times the number affected in 1985.\(^1\) Disturbingly, recent estimates suggest that 1 in 3 children born in 2000 will eventually develop diabetes.\(^2\) The consequences are devastating: diabetes causes one amputation worldwide every 30 seconds; it is a leading cause of blindness and kidney failure, with costs soaring to 132 billion dollars in 2002.\(^3,4\) Bleak news but there is reason to rejoice - diabetics who control their blood sugar levels reduce their risk of complications to levels similar to healthy counterparts.

What is diabetes?

Diabetes is the most common endocrine disorder. It is characterized by the inability of insulin to carry out its function. In type one diabetes mellitus, insulin cannot be produced while in type 2 diabetes mellitus - which affects 90% of diabetics - cells in the tissues and organs become insulin resistant.

Without insulin, cells are incapable of using glucose. This leads to elevated blood glucose levels while intracellular glucose becomes depleted. The consequences of diabetes stem from this shift in the distribution of glucose, the main energy source for cells. Without the action of insulin, the cells starve even in the overabundance of glucose in the blood: "Starvation Amidst Plenty". Simply put, diabetes is what happens when your cells are besieged. Inadequate insulin activity blockades glucose, which leads to inadequate cellular energy and a complete imbalance in metabolism, forcing your body into starvation mode, impeding the body systems function, causing a loss of homeostasis, which all promote disease. Appetite is stimulated, glucose stores in the liver are released, excess glucose in the blood is expelled in the urine leading to dehydration, tissue proteins are broken down as a fuel source and fat stores are accessed as an alternative fuel supply. Dehydration is especially harmful to the nervous system. Tissue protein breakdown leads to muscular wasting. Fatty acid utilization as a fuel source leads to the release of acidic ketone bodies that may cause metabolic acidosis and diabetic coma.\(^6\) Continuous exposure to elevated glucose levels leads to tissue alteration, increasing the likeliness of cataract formation, nerve failure, digestive problems and predisposes individuals to develop cardiovascular complications such as poor peripheral blood flow, ulcer formation, myocardial infarction, kidney damage and retinal injury.
The emergence of diabetes

There is a strong genetic component to type 2 diabetes with concordance of the disease in identical twins in 90% of cases. The cause behind diabetes is poorly understood but the disease is a clear illustration of why it is important to take care of ourselves. We all know that we should exercise, avoid refined carbohydrates and saturated fats and maintain a healthy weight. Yet according to the Center for Disease Control, more than half of the US adult population does not get enough exercise. Epidemiological evidence shows that dietary intake of refined carbohydrates such as corn syrup has quadrupled while fat consumption has increased by nearly 30% from 1963 to 1997. Weight control is becoming an increasingly common problem and the rates are climbing rapidly to the point where obesity is the number one health problem in the United States, affecting over 60% of the adult population. Insulin resistance as seen in type 2 diabetes is largely acquired and is a lifestyle-related disorder closely associated with poor dietary habits, lack of physical activity and obesity.

Dietary Habits and Diabetes

The glycemic load of food refers to the amount of glucose the tissues in the body are exposed to after a certain food is ingested. Foods associated with a high glycemic load result in a greater tissue exposure to glucose. Several studies have documented that a diet producing a high glycemic load is strongly associated with the development of type 2 diabetes mellitus and may even be the source of the condition.

The glucose fatty-acid cycle

- Inhibit glucose utilization
- Increase the release of glucose from stores in the liver
- Prolonged elevations reduce insulin secretion from the pancreas
- Lead to insulin resistance

A closer look at dietary patterns denotes the influence of a high glycemic load and excess fat consumption on the onset of diabetes. Epidemiological evidence reveals that refined carbohydrate consumption and high meat intake are both correlated with the incidence of diabetes and obesity. On the other hand, the presence of fiber in the diet and fruit and vegetable content prevents the development of the disease. No specific constituent of the diet is solely responsible for the emergence of diabetes but the overall quality of the diet is paramount to diabetes prevention.
Physical Activity and Diabetes

Exercise improves glucose metabolism and insulin sensitivity thereby reducing the risk of diabetes and heart disease. The US Diabetes Prevention Program study demonstrated that 30 minutes of daily physical activity and a 5-10% body weight loss resulted in a 58% reduction in the risk of developing diabetes. Another study performed by the Department of Endocrinology in Beijing looked at the impact of diet and exercise on the development of diabetes in patients with impaired glucose tolerance showing a 46% reduction in the risk of developing diabetes with exercise alone.

Obesity and Diabetes

The rate of obesity in US adults continues to increase. This trend will potentially lead to a decline in life expectancy for upcoming generations. Obesity increases the risk of heart disease and diabetes, two of the most common health problems in North America. Visceral adiposity (the presence of fat around the core) decreases insulin secretion and increases peripheral insulin resistance. Two follow-up studies have demonstrated that an elevated body mass index (a measure of weight distribution) increases the risk of developing diabetes by a factor of 20. In obesity, the presence of excess fat in the tissues leads to lipotoxicity — the accumulation of fat in organs that leads to cellular dysfunction and metabolic anomalies such as glucose intolerance.

The prevention of diabetes is no different than the prevention of most chronic and degenerative conditions. Sound nutrition, exercise and a healthy lifestyle go a long way when it comes to the maintenance of healthy blood glucose and for those predisposed to soaring blood sugar levels, prevention is vital. Natural treatments to prevent and address insulin resistance are constantly emerging. Nutrients such as isothiocyanates from hops, corosolic acid from banaba, β-glucans from oats and hydroxychalcone from cinnamon improve insulin sensitivity, lower blood glucose levels, reduce the glycemic index of food, improve blood lipid profiles and improve outcome in diabetics.

References

21 Ibid.
33 Slowik M, Vidali-Puig AJ. Lipotoxicity, overnutrition and energy metabolism in aging. Ageing Res Rev. 2006 Apr 19
Isohumulones: Peroxisome Proliferator activators

Isohumulones are bitter compounds from hops and are responsible for the bitter taste of beer - where they are found in minute concentrations. Isohumulones have been shown to improve blood lipid profiles and glucose levels in mice and have ameliorated hemoglobin A1c and blood glucose levels in mildly diabetic patients. The health benefits associated with Isohumulones are imparted by their ability to bind to and activate peroxisome proliferator-activated receptors (PPAR) and . PPAR are cellular receptors sensitive to blood lipid levels which allow the transcription of certain genes responsible for lipid utilization and breakdown. This is a significant benefit for diabetics because the metabolism of free fatty acids and sugar are closely related. Indeed, free fatty acids compete with glucose and elevations in free fatty acid levels prevent the entry of glucose into cells. This phenomenon through which fat inhibits glucose utilization is known as the glucose fatty-acid cycle and is central to insulin resistance as seen in diabetes type 2.

Activation of the PPAR leads to the cellular production and activation of a wide range of enzymes that are required for the utilization of fatty acids. In turn, these enzymes improve lipid metabolism, lower circulating levels of lipids, and improve insulin sensitivity. Activation of the PPAR is an ideal target for diabetics because the activation of the receptor improves insulin sensitivity, lowers blood lipid levels and may even have a weight-lowering effect.

Isohumulones activate both PPAR and . Treatment with isoohumulones in mice prevented the development of diabetes, reduced plasma triglyceride levels by 62%, free fatty acid levels by 73% and plasma glucose levels by 65%. The same animal study also demonstrated that supplementation with isoohumulones prevents the onset of insulin resistance in high fat diets. Similar ameliorations in blood lipid profiles were confirmed in another animal study with demonstrated reductions in triglyceride levels. Isoohumulones have also been shown to increase HDL-cholesterol in mice. HDL-cholesterol is the fraction of cholesterol that has a protective effect on the development of arterial plaque. Furthermore, the addition of isoohumulones to the diet leads to weight reductions in animal studies. Preliminary studies in diabetic patients have been very promising with significant reductions in both glycated hemoglobin and blood glucose levels.

Reduce your glycemic load with β-glucans

The health benefits of dietary fiber are considerable. Fiber slows down the gastrointestinal absorption of food, reduces the glycemic load of a meal, reduces cholesterol levels and is an important factor in feelings of satiety. All of those factors are essential in the maintenance of normal blood glucose levels.

β-glucans:
- Slow down absorption
- Reduce the glycemic index of food
- Diminish blood glucose levels
- Lower blood cholesterol levels
- Help regulate appetite

β-glucans are large polysaccharides that cannot be digested. They absorb water and become viscous. The health benefits associated with β-glucans are related to their viscosity. Indeed, they bind to bile salts in the small intestine.
intestine preventing the reabsorption of cholesterol. A significant payback as elevated fatty acid levels decrease glucose utilization eventually leading to insulin resistance.

Tissue exposure to elevated glucose concentrations increases the risk of developing diabetes. Refined sugars and processed cereal grains are more and more prevalent in developed countries. Their rapid breakdown and quick absorption leads to a higher tissue exposure to glucose and a corresponding elevation of insulin produced by the pancreas, eventually leading to metabolic disorders such as type 2 diabetes, obesity and cardiovascular disease. ß-glucans interfere with carbohydrate absorption, reduce gastric emptying and slow down the digestion and absorption of food, lowering the glycemic index of foodstuff (a measure of a food’s effect on blood sugar).

Two separate clinical studies have demonstrated that ß-glucans reduce plasma glucose and insulin levels after a meal.

Corosolic acid

Corosolic acid is extracted from banaba. The extract contains a polyphenol known for its glucose lowering effect. Supplementation with the extract has reduced blood sugar elevations in animal studies and two recent clinical trials in humans have established the extract’s effectiveness at improving glycemia. The latest study on corosolic acid looked at the ability of the extract to improve blood glucose levels after a glucose tolerance test (a test designed to evaluate the body’s response to glucose). A significant improvement was revealed 90 minutes after the individuals were given 75 g of glucose.

Cinnamon

New research supports the efficacy of cinnamon for healthy glucose maintenance. Known as a spice in Western countries, cinnamon is used as a medicine in Asia. Cinnamon mimics and amplifies the effects of insulin and helps to regulate blood glucose and improves glucose utilization. Cinnamon contains a hydroxychalcone known as the cinnamon methylhydroxychalcone capable of up regulating glucose uptake and glycogen synthesis by cells. Both processes are essential for blood sugar regulation. Cinnamon may also help reduce blood lipid levels through its action on the liver. Two human studies in diabetics have shown a significant improvement with cinnamon supplementation. In the first study blood glucose levels dropped by 18-29%, triglycerides levels were reduced by 23-30%, LDL cholesterol lowered by 7-27% and total cholesterol by 26% after 40 days of cinnamon supplementation in patients with poorly controlled type 2 diabetes. In the second study, 4 months of supplementation with a cinnamon extract in diabetes patients led to a moderate but significant reduction in blood glucose levels; decreases were above and beyond the reductions achieved through diet and medication alone.

Cinnamon

- Activates insulin receptors
- Increases cellular glucose uptake
- Enhances glycogen production (glycogen is stored glucose)
- Potentiates the action of insulin

Rapid Aging

Diabetes is often referred to as the disease of "rapid aging". The pillar of disease prevention is the maintenance of normal tissue and optimal metabolic function. In essence, disease prevention strives to extend life through healthy lifestyle and dietary habits which in turn maintain strong blood vessels, encourages normal cellular differentiation, gives rise to optimal cognition and incites normal metabolism and glycemia. Enough is known about diabetes to curb the onslaught of the disease. The benefits of natural treatments with demonstrated efficacy in the maintenance of normal blood glucose levels should not be overlooked.
References

13 Chetty VT, Sharma AM. Can PPARgamma agonists have a role in the management of obesity-related hypertension? Vascul Pharmacol. 2006 May 17
The Aging Process

We are the longest living mammals. The maximum life expectancy for humans is roughly 120 years and it is believed that our genetic potential should allow all of us to live over 100 years. Life expectancy has increased dramatically in the industrialized world during the 20th century from roughly 40-45 to nearly 75 years, but few make it to 90, never mind 100. The longest living group of humans is Japanese women with a life expectancy of 83 years. Living longer is not always better and many elders are plagued by degenerative diseases such as osteoporosis, cardiovascular problems, cancer, cataracts and arthritis. At present, the only methods known to increase lifespan are better lifestyle choices, and the prevention and treatment of disease, but what if we could influence the aging process itself?

The aging process is still largely a mystery. We age because natural selection chooses which genes will be propagated and which genes will be selected against. Unfortunately, genes that affect us after we have reproduced cannot be selected against and are passed on. Aging is a gradual decline in organ function, a loss of tissue structure and an accumulation of cellular damage. We all age differently; the timing, progression and consequences vary from person to person. The mechanism behind the aging process is not completely recognized but mounting research has provided clues, ideas and theories.

Free radicals are certainly part of this puzzle. They injure our tissues and every cell in our body is exposed to their damaging effect. Unfortunately, free radicals are by-products of our breathing and completely preventing their formation is unrealistic. Antioxidants on the other hand quench free radicals and prevent some of the damage they induce.

Another possibility that could limit lifespan is our cells ability to divide. It is thought that our cells might only be able to divide a certain number of times. That number might be programmed in our genome. Our cells losing their ability to partition would weaken our immune system and slowly lead to a loss of organ function and a breakdown of metabolic reactions.

Another chemical process that occurs in our body and leads to significant tissue injury and loss of function over time is known as the Browning Reaction, or the formation of Advanced Glycation End products (AGE) - the permanent glycation of proteins. It is the same reaction that occurs in the food we eat, toasted bread for instance becomes brown because of this reaction. In our body, the reaction occurs when protein and sugar molecules bind together. This results in loss of function and poor gene expression. Permanent protein glycation leads to the formation of cataracts, atherosclerosis, and other diseases common later in life. The Browning theory of aging was first brought forth in the 1980s by Monnier and Cerami.1

Glycation is especially rapid in diabetes because of the increased presence of glucose and is the reason why diabetes is sometimes referred to as “accelerated aging”. For example, cataracts occur, on average, 10-15 years earlier in diabetics and are predictors of early death in such subjects.2-3-4 Atherosclerosis, myocardial infarction, strokes, joint stiffness, reduced lung elasticity, hypertension, osteoarthritis and infections are all more common in diabetic patients.5 Protein glycation is a process that occurs spontaneously, no enzymes are required and it ultimately leads to the formation of intermolecular cross-links. This leads to loss of function and increased stiffness and is
especially problematic for more vulnerable tissues such as the kidneys, capillary basement membranes and the cardiovascular and pulmonary systems.

**AGE and ALE formation**

The French chemist L. C. Maillard first reported the formation of a yellow brown substance when he heated amino acids with sugars. That was in 1912 and the process is now known as the Maillard reaction, i.e. non-enzymatic glycation or the browning reaction. Non-enzymatic glycation does not occur only in foods, it is a common reaction that occurs in our body when proteins and sugar molecules bind together. This interaction was first observed in the 1970's when it was discovered that hemoglobin could be non-enzymatically bound to glucose. We also know that as hemoglobin ages and as blood glucose levels rise, the degree of glycation increases. It was later discovered that tissues that rejuvenate slowly such as collagen and crystallins are most vulnerable to AGE formation. However the most damaging AGE reactions affect DNA; the blueprint for the production of all proteins found in the human body. Once DNA has been affected, the appearance and configuration of proteins may be compromised. The damage is accelerated by hyperglycemia in diabetes, by hyperlipidemia in atherosclerosis and by oxidative stress in chronic disease. Glycation occurs when the free amino groups of lysine, hydroxylysine or arginine residues, as well as amino groups of phospholipids and guanyl nucleotides of DNA are spontaneously reduced by sugars such as glucose and its metabolic intermediates: triose phosphates, glyoxal and methylglyoxal. Any tissue containing those residues and amino groups is prone to protein glycation. The initial reaction of a sugar molecule with a protein leads to the formation of free radicals. Reactive Oxygen Species:

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<td>H$_2$O</td>
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</tr>
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<td>ROO·</td>
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<td></td>
<td>HOCI</td>
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formation of a Shiff base that rearranges itself to form a ketoamine. The covalent bonding of a sugar and an amino acid leads to the production of an Amadori product. Subsequent reactions lead to the formation of AGE. A reaction similar to AGE formation can also occur through lipid peroxidation and metal-catalyzed glucose auto-oxidation (referred to as advanced lipoxidation end products or ALE). The glycation of proteins to early glycation products is reversible. Shiff bases and Amadori products are produced through reversible reactions. However, AGE are stabilized through irreversible reactions such as rearrangement, dehydration and condensation.

Interestingly, of all the naturally occurring sugars, glucose has the slowest rate of glycation and AGE formation. The rate of AGE formation by sugars such as fructose, glucose-6-phosphate and glyceraldehyde-3-phosphate is far more rapid than for glucose. For example, fructose-fed rats had blood glycated hemoglobin levels that were significantly higher (43%) than controls.

Several factors contribute to protein glycation in the body. Smoking and diet are important contributors to AGE formation but there are still many unknowns and new AGE are still being discovered. Recent studies suggest that genetic factors also have an important influence on circulating AGE levels. Once AGE are formed, they remain in the tissue until the protein from which they are formed is degraded. Therefore, AGE accumulate most in tissues where protein turnover is slow. Such tissues include the crystallin in the lens of the eye and the collagen found in connective tissue.

AGE and Longevity

It is difficult to understand the full extent of the impact AGE formation has on health because we do not have very good methods of identifying AGE. Many AGE are unstable in acids or alkaline solutions typically used to hydrolyze and study proteins. This makes it difficult to recognize and study them. Some AGE can only be identified after proteolysis of the protein. New AGE’s are being discovered and it is clear that carbohydrates are not the only way proteins are chemically modified. For instance, advanced lipoxidation end products (ALE) are the result of the interaction of lipids and proteins. It is apparent that AGE formation is only a part of protein modification in tissues.

AGE concentrations correlate with age but not with lifespan and some have criticized the glycation theory of aging based on this observation. The levels of AGE in the proteins of old short-lived animals cannot be compared to the levels of AGE found in old long-lived animals. It is important to
understand that AGE bioaccumulate in tissues with slower protein turnover times. AGE formation might be similar in different tissues - for instance, in skin and collagen - but the half life for collagen is 120 years versus 15 years for skin. It is therefore not surprising that the levels of the AGE/ALE compounds CML, CEL and pentosidine are three times higher in human articular collagen versus skin collagen of the same age. Therefore, AGE concentration in tissues correlates with age but not life span. However, AGE may influence longevity through another injurious mechanism; their impact on our genome.

In a paper published in the Annals of the New York Academy of Sciences, John W. Baynes puts forth a very interesting explanation for the apparent discrepancy between tissue concentration of AGE and longevity. AGE could exercise their effect on longevity through their action on DNA. There is evidence to support that DNA can be glycated by AGE and ALE which explains why patients with end-stage renal failure who have increased levels of AGE have a high incidence of DNA damage. DNA damage occurs through the interaction of AGE and ALE with groups found on the amino portion of adenine and guanine residues found in the DNA matrix. The formation of AGE in the genome would alter the DNA sequence and would lead to cellular apoptosis, necrosis, chronic diseases and increased rates of cancer. The impact of AGE on DNA is relative to the rate of glycation but the consequences would be influenced by the efficiency of DNA repair - a process that is less efficient in shorter-lived species. Although AGE formation contributes to DNA damage, it is the efficiency with which the organism can repair and reverse this damage that controls the rate of the aging process and the longevity of the animal. In humans and other long-lived organisms, the damage associated with the Maillard reaction is averted more efficiently through complex protection mechanisms. The availability of metal ions that promote glycation reactions is restricted, detoxification pathways remove and inactivate reactive intermediates and antioxidant mechanisms prevent injury induced by reactive sugars. In other words, there are two important factors in the maintenance of biological integrity: the rate at which injury is incurred and the organism’s efficiency at recovering from this onslaught. Short-lived species incur less damage throughout their life span but they are short-lived because they cannot repair this damage as effectively as long-lived organisms.

There is growing evidence that suggests that the accumulation of Advanced Glycation End products is involved in a variety of diseases and degenerative disorders. AGE are formed in surplus in diabetes, renal failure and with advancing age. We have known for years that continuous cellular exposure to excess glucose prevents normal growth, which leads to significant tissue dysfunction and has been related to several degenerative diseases. The increased presence of carbonyl compounds and glycated proteins lead to the inhibition of key cellular enzymes. These include: glyceraldehyde-3-phosphate dehydrogenase (GAPDH)-an important enzyme in glycolysis and apoptosis which may be involved in Alzheimer’s and prostate cancer progression, glutathione reductase - an enzyme that recycles glutathione and lactate dehydrogenase - involved in cellular energy production. The formation of Advanced Glycation End-products is especially prevalent in diabetes and has been related to the development of diabetic complications such as vascular disease, retinopathy and impaired wound healing. Elevated glucose levels lead to the binding of sugar molecules to albumin. This interferes with the normal functioning of the protein and contributes to diabetic
complications. Even short periods of hyperglycemia appear to be sufficient to increase the formation of α-oxoaldehyde, a significant product in early glycation. AGE are toxic to neurons and may be an important factor in the development of diabetic neuropathy because they activate the enzyme nitric oxide synthase, which may cause the death of neurons. Furthermore, AGE negatively affect energy production and lead to decreased cellular ATP levels, increase glucose consumption and lactate production in neurons.

Diabetic patients are at an increased risk for cardiovascular disease. They are predisposed to certain risk factors such as hypertension and abnormal blood lipid profiles. The presence of AGE in the vasculature was shown to be related to hypertension and the long-term administration of an AGE inhibitor reduces blood pressure. In addition, epidemiological evidence demonstrated that hyperglycemia is a risk factor for heart disease: the lower the blood sugar levels, the lower the cardiovascular disease risk. Diabetic blood vessels contain more AGE, display fewer Receptor of Advanced Glycation End-product (RAGE) and produce more proinflammatory cytokines. Diabetic patients were shown to have, on average, a 12.6% increase in AGE plasma levels and up to 46.5% increases when faced with kidney damage. This has serious implications for atherosclerosis because glycation impedes normal cellular growth and prevents the normal healing of blood vessels. In a study on diabetic animals, an AGE cross-link breaker prevented the development of arteriole plaque by 30% and an AGE inhibitor led to a 40% reduction in plaque formation. Similarly, diabetic patients were shown to have higher levels of glycated LDL cholesterol, an especially harmful type of cholesterol, thought to be a useful indicator of heart disease risk.

Another common pathology where AGE formation appears to have a significant impact is Alzheimer’s disease (AD), a degenerative brain disorder currently affecting 4.5 million Americans. Accumulation of AGE leads to cellular cytotoxicity and since AGE levels are higher in AD, it is possible that they may contribute to the cell death seen in AD. It has also been shown that nucleotide (the building blocks for DNA and RNA) glycation leads to mutations and programmed cell death. AGE formation promotes protein aggregation that is linked to amyloidoses such as Alzheimer’s disease and familial amyloidosis. The finding that patients with diabetes have a significantly higher risk of developing Alzheimer’s disease supports the involvement of AGE formation in Alzheimer’s.

In human cartilage, the presence of AGE increases 50 fold between the age of 20 and 80. The strength of connective tissue comes from the intermolecular collagen crosslinks. AGE formation in the collagen matrix prevents such crosslinks and the accumulation of AGE in cartilage leads to increased stiffness and brittleness. Moreover, AGE hinders normal tissue turnover. In cartilaginous tissues for instance, AGE prevents proteolytic degradation, which promotes the further accumulation of AGE. This partly explains why the most important risk factor for the development of osteoarthritis is the age of the individual; the older the tissue, the more AGE.

The glycation of collagen is also an important factor in the loss of bone quality seen with advancing age. Studies have shown that AGE accumulation in the cartilaginous portion of the bone matrix leads to a 40% decrease in cellular proliferation, interferes with cellular adhesion to the extracellular matrix and obstructs genetic expression. As AGE increases in cartilage, proteoglycans and collagen synthesis in articulations decrease. A recent study has shown that with increasing AGE concentrations, glycosaminoglycan loss was also increased, repair was impeded and the uptake of new proteoglycans into the collagen matrix was reduced. In this study, damaged knees were injected with ribose to increase AGE formation. The release of glycosaminoglycans was increased by a factor of four and there was a 40% increase in articular damage. Ribose injections led to a significant augmentation in cartilage degeneration. AGE also promotes chronic inflammation through its effect on cytokines and free radical production.

A recent study has shown that with increasing AGE levels in articular tissue, osteoarthritis severity also increases.

It is unequivocal that AGE are associated with age-related disorders such as arteriosclerosis, inflammatory disorders, diabetes, arthritis and neurodegenerative conditions. After all, AGE leads to protein denaturation, genetic mishaps, enzyme inactivation and an inadequate or misdirected immune response. Research into anti-AGEing compounds and newer therapies to address and prevent glycation and lipoxidation may prevent age-related disorders and might prove useful for the treatment and prevention of conditions for which adequate therapies are currently lacking.
Preventing Glycation

The prevention of glycation would lead to significant improvement and a reduction of complications seen in diseases such as diabetes where the formation of AGE leads to significant health problems. More importantly, because no level of AGE in any bodily tissue should be considered harmless; thwarting this process would lead to health improvements and would fend off the loss of function seen in aging.

We possess an enzymatic defense against protein glycation but this defense system is imperfect as glycation occurs under normal physiological states. The enzymes involved in the prevention of glycation are glyoxal I, specific aldehyde reductases, dehydrogenase isoenzymes, amadoriase and fructosamine 3-deoxyglucosone. It is important to realize that free radicals and oxidative stress promote glycation because the depletion of glutathione and NADPH by oxidants reduces the activity of glyoxalase I. Also, some aldehyde reductase are NADPH dependent.

Several natural compounds and pharmaceutical drugs have been investigated for their possible efficacy in the prevention of protein damage by sugars or lipids. Unfortunately, test tube experiments are often misleading because it is difficult to differentiate between inhibition of carbohydrate auto-oxidation and AGE inhibition. Fortunately, there is reason to be optimistic: clinical studies have clearly demonstrated that protein glycation and lipoxidation can be avoided.

The Nutritional Shield

Most degenerative processes in the human body can be delayed or prevented through better nutrition and wiser lifestyle choices. Better nutritional and lifestyle habits remain the best approach to prevent disease and they are partly responsible for the extended lifespans seen in recent years. It should be no surprise that two powerful anti AGEing products are in fact vitamins. Benfotiamine (a form of vitamin B₁) and pyridoxamine (a form of vitamin B₆) have been studied extensively for their ability to prevent the formation of AGE and ALE. The results speak for themselves.

Benfotiamine

Thiamine, also known as vitamin B₁, was initially recognized as an anti-beriberi factor. Beriberi comes from a Sinhalese word meaning extreme weakness. The disease was primarily seen prior to the 19th century. Casimir Funk isolated the anti-beriberi factor from rice in 1912. It was the first compound referred to as a vitamine; an amine essential for life, hence its designation as vitamin B₁. The chemical formula for vitamin B₁ was recognized by Robert R. Williams in 1931, and was named thiamine. The body’s thiamine stores are small (only 30 mg) and because the vitamin has a central role in energy production, most stores are located in muscles. The active form of the vitamin is thiamin pyrophosphate (TPP). Common indications for the vitamin include the treatment of nerve disorders, and the prevention of deficiency in disorders such as alcoholism, cirrhosis, gastrointestinal disease, increased carbohydrate intake, hyperthyroidism and infection. In a more recent study, thiamine supplementation in 120 young adult women improved decision time and mood. The vitamin is also useful for the prevention and for the treatment of heart failure.

Thiamine is needed for several enzymatic reactions in the human body. The most important being the vitamin’s involvement in pyruvate dehydrogenase (an enzyme important in energy production), transketolase (an enzyme involved in lipid, glucose and branched chain amino acid metabolism and also for the production and maintenance of the myelin sheath surrounding nerve cells), and 2-oxoglutarate dehydrogenase (involved in the synthesis of acetylcholine, GABA and glutamate).

Benfotiamine is a newer, highly absorbable, fat-soluble source of vitamin B₁. It has similar application to thiamin but it is roughly 5 times more absorbable than regular thiamine and can pass directly through cell membranes. It is better assimilated, enters tissues with more ease and has longer periods of tissue retention. It is thiamine’s newer cousin and was developed in Japan in the 1950’s for the treatment...
**SUPPLEMENT FACTS:**

**Serving Size:** 9 Capsules

**Phytonutrient Complex**

- Calcium D-Glucarate: 15 mg
- Chlorophyllin Complex: 300 mg
- Trans-resveratrol (Chirally Pure): 1.8 mg
- Indole-3-Carbinol (I3C): 20 mg
- Sulforaphane: 7.1 mg

**Vitamins**

**Vitamin A Complex**

- Retinol (palmitate): 500 IU
- Natural-Source Mixed Carotenoids:
  - Alpha-carotene: 1332 IU
  - Beta-carotene: 9990 IU
  - Cryptoxanthin: 25 IU
  - Lutein: 6.7 mg
  - Lycopene: 18 mg
  - Zeaxathin: 54.5 mcg

**Vitamin B Complex**

- B1 (Thiamine): 9 mg
- B2 (Riboflavin): 2.5 mg
- B3 (Niacin from Inositol Hexanicotinate): 11.5 mg
- B6 (Pyridoxine): 100 mg
- B7 (Pyridoxine): 25 mg
- B12 (Cyanocobalamin): 24 mcg
- Biotin: 800 mcg
- Pyrroloquinoline quinone (PQQ): 30 mcg
- Choline (Bitartrate): 500 mg
- Inositol: 100 mg

**Vitamin C Complex**

- Vitamin C (Magnesium Ascorbate): 400 mg
- Mixed Citrus Bioflavonoids: 100 mg
- Quercetin: 65 mg
- Vitamin D3 (Cholecalciferol): 1000 IU

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Formulated with a broad spectrum of vitamins, minerals, and phytonutrients whose role in supporting your health is backed by scientific research in humans, Ortho•Core is the most advanced, balanced, and comprehensive core nutritional supplement ever! Optimal forms and science-driven dosing make Ortho•Core a solid cornerstone on which to build your unique nutritional supplement regimen.

### Vitamin E Complex

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<tr>
<td>alpha-tocotrienol</td>
<td>10 mg</td>
</tr>
<tr>
<td>beta-tocotrienol</td>
<td>3 mg</td>
</tr>
<tr>
<td>gamma-tocotrienol</td>
<td>0.1 mg</td>
</tr>
<tr>
<td>delta-tocotrienol</td>
<td>6 mg</td>
</tr>
</tbody>
</table>

| Vitamin K₂ (As Menatetrenone (MK-4)) † | 500 mcg |

### Minerals

| Boron (Citrate) | 1.8 mg |
| Calcium (Citrate-Malate, D-Glucarate) | 300 mg |
| Chromium (Picolinate) | 100 mcg |
| Copper (Citrate) | 1.5 mg |
| Iodine (Potassium Iodide) | 150 mcg |
| Lithium (Orotate) | 1000 mcg |

| Magnesium (Citrate, Aspartate, Oxide, Ascorbate) | 210 mg |
| Manganese (Glycinate) | 2.3 mg |
| Molybdenum (Na Molybdate) | 45 mcg |
| Selenium (Se-Methylselenocysteine) | 200 mcg |
| Silicon (Na Metasilicate) | 50 mg |
| Strontium | 1.5 mg |
| Vanadium (Citrate) | 18 mcg |
| Zinc (Citrate) | 11 mg |

### Biotransformation Conjugates

| Acetic acid | 100 mg |
| Glycine | 400 mg |
| Taurine | 500 mg |
| Trimethylglycine (TMG HCl) | 500 mg |
| N-Acetylcysteine (NAC) | 200 mg |

The Complete E-Complex, instead of a reliance on overweighted “natural” alpha-tocopherol or “mixed tocopherol” ratios that drive other E vitamers out of your tissues and rob you of their benefits.

Boron is not just for women! Recent epidemiological and experimental studies link this mineral to healthy prostate cell growth and differentiation.

Lithium is a mineral, not a drug. Recent research has revealed lithium’s neuroprotective powers and has shown that dietary lithium intake supports normal mood balance.

Magnesium blended for good bioavailability with reasonable capsule count.

Selenium as Se-methylselenocysteine (SeMC): the most vigilant form of this guardian of cellular health.

Silicon, Strontium, and Vanadium: missing from most multis, these minerals’ nutritional significance is rapidly emerging. Dosages reflect what’s found in good diets and mineral-rich drinking water.

Zinc and Copper in the balance needed for health. Unbalanced zinc supplementation usurps copper’s biochemistry, with long-term consequences for your health.

Biotransformation Conjugates needed to depolarize and excrete activated xenobiotic chemicals.

† USA version only
of vitamin B1 deficiency. This modern form of the vitamin holds promise against a new threat, AGE/ALE formation. Benfotiamine can prevent protein glycation/lipoxidation and lessen the damage they cause to cellular structures. These properties are unique to benfotiamine and are not seen with regular thiamine. The vitamin exhibits antioxidant activity and, based on its structure, is considered an AGE breaker. Studies performed on human umbilical vein cells cultured in a high glucose environment demonstrated that the addition of benfotiamine to the solution reduced AGE production to levels similar to the ones expected under normal physiological glucose.

Thiamin, however, does not prevent AGE generation in diabetic rats. In a study performed on diabetic rats where nerve conductivity and nerve glycoxidation were assessed with thiamine and benfotiamine supplementation, the results clearly showed that benfotiamine is a superior AGE inhibitor. Three months after diabetes induction, nerve conductivity dropped by 10.5% and the glycation product CML rose by 3.5 fold and deoxyglucosone AGE formation was increased by 5.1 fold. After six-months of supplementation with benfotiamine, nerve conduction velocity was almost normal. Thiamine supplementation also improved nerve impulse transmission but not to the extent of benfotiamine. More importantly, benfotiamine completely prevented diabetes induced CML products whereas thiamine did not significantly reduce AGE levels. Another study in 14 patients suffering from diabetic polyneuropathy (nerve damage manifesting as pain, tingling, or numbness) showed that a combination of benfotiamine and vitamin B6 for 6 weeks significantly reduced pain from an intensity of 8.2 to a score of 2.3. Also of significance, supplementation led to enhancement in vibratory sensitivity and general improvements in 93% of cases.

Another study examined benfotiamine’s effect on diabetic red blood cells. The results are impressive: 40% reductions in CML levels and intracellular methylglyoxal derived AGE dropped by almost 70%

Benfotiamine corrected defective cellular replication and reduced AGE generation. The vitamin also prevented diabetic retinopathy in diabetic rats preventing an increase in the number of acellular capillary segments in the retina (see figure 1). Acellular capillary segments are the result of the vascular endothelium no longer being able to proliferate and repair itself.

Benfotiamine’s effectiveness in the prevention of AGE formation may be related to the normalization of glycolysis. Accelerated glycolysis leads to the production of more intermediate metabolites such as glyceraldehyde-3-phosphate (G-3-P) and fructose-6-phosphate, which are highly reactive with proteins (G-3-P is 200 times more reactive to proteins than glucose). Also, in hyperglycemic states, the mitochondria releases an excessive amount of superoxides - reactive oxygen compounds that can cause significant damage to cells. Those superoxide then inhibit the glycolytic enzyme GAPDH which forces glycolysis metabolites into four other glucose pathways, causing hyperglycemic damage. Benfotiamine activates the enzyme transketolase, which transforms glucose metabolites before they can interact with proteins.

Benfotiamine has been used for more than 12 years in Europe and has an impeccable safety record. It is an important ally in the fight against glycation/lipoxidation and has proven to be an effective vitamin for diabetics and shows promise as an anti-aging therapy.

**Pyridoxamine**

Vitamin B6 is important for numerous metabolic functions. The vitamin is needed for over one hundred enzymes involved in the metabolism of proteins, for the production of neurotransmitters, antibodies and red blood cells. Common indications for vitamin B6 include the treatment of homocystinuria (a metabolic abnormality characterized by excessive amounts of the amino acid homocysteine in the

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**Figure 1: Effect of benfotiamine on experimental diabetic retinopathy.** a, Photomicrographs of retinal vessels prepared from non-diabetic (left), diabetic (middle) and benfotiamine-treated diabetic (right) rats. b, Quantitation of acellular capillary segments in retinal vessels from non-diabetic, diabetic and benfotiamine-treated diabetic rats. *P < 0.01 compared with non-diabetics. Twelve retinas were analyzed morphometrically from each group. For each assessment, 10 fields per retina were randomly selected. Used with permission
urine), premenstrual syndrome, imbalances due to oral contraceptives (oral contraceptives can impair vitamin B₆ status), and impaired glucose tolerance in pregnancy. It also has exhibited immuno-stimulating properties. General signs of a vitamin B₆ deficiency include, microcytic and hypochromic anemia, depression, dermatitis and confusion. There are several forms of vitamin B₆: pyridoxine, pyridoxal and pyridoxamine. Vitamin B₆ deficiency is common and varies depending on demographics. (See Table 1)

Pyridoxamine is a form of vitamin B₆. It is both an AGE inhibitor and an AGE breaker. Pyridoxamine traps AGE/ALE and it cleaves the model AGE crosslink phenylpropanedione. Pyridoxamine is thought to trap reactive carbonyl-precursors to AGE that are a result of oxidative and non-oxidative chemistry. Pyridoxamine performs this function more efficiently than other forms of vitamin B₆. Pyridoxamine is extremely reactive with 1,4-Dicarbonyl compounds, which exhibit toxicity through their reactivity with lysyl residues. A reaction that leads to the formation of AGE. Pyridoxamine binds to carbonyl compounds at a rate that is 2300 times faster than N-acetyllysine, which means that it is far better at binding carbonyl compounds than lysine. Lysine will be spared if pyridoxamine is present in sufficient amounts. Pyridoxamine can also bind to methylglyoxal, another dicarbonyl compound involved in AGE formation. This reaction leads to the formation of a methylglyoxalase-pyridoxamine dimer. It was shown that with proper supplementation, plasma pyridoxamine could reach levels sufficient to react with all the methylglyoxal present in plasma. Additionally, it has recently been suggested that pyridoxamine might cleave AGE because it was shown that it could cleave phenylpropanedione, a model for permanently glycated proteins. This is a significant finding; pyridoxamine can prevent AGE and ALE formation, but it also appears to have the capability to reverse some of the damage already incurred to bodily proteins. Pyridoxamine can prevent the formation of glycation end products from free sugars but can also reverse the early stages of glycation. Pyridoxamine is known as an Amadorin because it can interrupt protein glycation in its latest stage - once the protein and the sugar molecules have formed an Amadori adduct but not an AGE molecule. Supplementation with pyridoxamine is especially beneficial for diabetics. It is a promising treatment for the prevention and improvement of nephropathy as seen in type 1 and type 2 diabetic animals. Pyridoxamine's capacity at preventing the formation of AGE avoids cellular damage

<table>
<thead>
<tr>
<th>Number of participants in study</th>
<th>% Deficient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young women embarking on contraceptive study</td>
<td>129</td>
</tr>
<tr>
<td>Elderly men undergoing prostate surgery</td>
<td>94</td>
</tr>
<tr>
<td>Preschool children</td>
<td>35</td>
</tr>
<tr>
<td>Breast-fed infants</td>
<td>84</td>
</tr>
<tr>
<td>Pregnant adolescents</td>
<td>122</td>
</tr>
<tr>
<td>Hospitalized elderly subjects</td>
<td>153</td>
</tr>
<tr>
<td>Hospital patients</td>
<td>650</td>
</tr>
<tr>
<td>Men, various ages</td>
<td>617</td>
</tr>
<tr>
<td>Free-living elderly subjects</td>
<td>198</td>
</tr>
<tr>
<td>Hospitalized elderly subjects</td>
<td>102</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>458</td>
</tr>
<tr>
<td>Adolescent girls</td>
<td>127</td>
</tr>
<tr>
<td>Low-income pregnant women</td>
<td>127</td>
</tr>
</tbody>
</table>

and prevents the chemical modifications of tissue proteins seen with aging. Pyridoxamine prevents lipid peroxidation and glycosylation of hemoglobin and increases the sodium-potassium ATPase activity in cells exposed to elevated glucose levels. Proper functioning of the sodium-potassium pump is essential for the normal activity of nerve and muscle cells. An in vitro study showed that pyridoxamine is a powerful free radical scavenger and that it could inhibit the formation of superoxide radicals seen with 30 mM and 50 mM solutions of glucose by 97 and 96 percent respectively. Vitamin B6 also prevented increases in levels of hemoglobin A1c and lipid peroxidation in red blood cells exposed to a high glucose environment. Pyridoxamine not only inhibited the formation of AGE/ALE, but it also demonstrated a strong lipid lowering effect in rats, retarded the development of renal disease, and delayed the onset of retinopathy. It has been suggested that lipid derivatives in the form of CML and CEL are a significant source of protein modification. In obese rats, pyridoxamine reduced the presence of those compounds in skin collagen. The prevention of glycation/lipoxidation by pyridoxamine is not related to glycemia because pyridoxamine has no effect on blood glucose levels. It is clear that pyridoxamine offers protection against the formation of AGE/ALE, which safeguards bodily proteins and prevents a wide range of pathologies seen with the normal aging process.

Pyridoxamine's absorption was carefully studied. The vitamin is absorbed through passive diffusion with 35% efficiency and has a plasma half-life of 2-3 hours. Vitamin B6 has been demonstrated to be safe in dosages up to 200 mg per day.

Getting through the door

This is all very complicated, but really quite simple. All proteins have a specific function and that function relates to their structure. If the protein becomes glycated, the structure changes and the function is lost. Imagine the protein structure as being a door with the function of letting people through. The key to the lock would represent the sugar molecule. Pyridoxamine and Benfotiamine can prevent the key from entering the lock by intercepting dicarbonyl intermediates which are precursors to the formation of AGE.

Another Orthomolecular Breakthrough for Diabetics

Not producing enough or the cellular inability to utilise insulin, wreaks havoc on the body. The usefulness and effectiveness of natural and nutritional interventions for those whose blood sugar levels have gone astray should not be overlooked.

Ortho-Glucose II™ contains isohumulones, hops, cinnamon, corosolic acid and chromium picolinate in doses supported by clinical research in type II diabetic patients. These nutrients and plant extracts have been shown to reduce blood sugar levels, potentiate the action of insulin and improve glucose utilization. But most importantly, Ortho-Glucose II diminishes the risk of complications associated with diabetes.

Ortho-Glucose II is the ideal choice for those trying to regain normal carbohydrate metabolism and striving to achieve normal blood glucose levels.

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
Where pyridoxamine stands apart is in its ability to remove the key once it has entered the lock - when protein glycation has occurred. Once the door is locked and the key is gone as in AGE formation, the only way through the door is to dismantle it. This is known in the body as protein or tissue turnover.

If you think that AGE/ALE formation is not a concern because your blood sugar levels are normal, you are mistaken. It is well know that circulating levels of Hb A1c - the product of the non-enzymatic glycation of hemoglobin with glucose - is normally roughly 4% of total hemoglobin. This level is 3-5 times higher in diabetics, but 4% is clearly a concern. If 4% of our weight is constituted of damaged tissue, it means that the average man carries 7lbs of dead weight, in this case comprised of harmful compounds that impede tissue function, stimulate inflammation, promote cellular dysfunction and lead to genetic mayhem. Furthermore, this example utilized glucose, a molecule that is far less reactive than other sugar molecules when it comes to protein glycation - that is why it was chosen through natural selection as the blood sugar molecule - any other sugar compound would probably have caused too much glycation for life to be maintainable. There are several molecules capable of non-enzymatic reactions with proteins. Sugars and lipids can interact with amino acid residues and new glycation reactions are constantly being discovered. It is likely that the total body burden of damaged proteins far exceeds 4%.

When it comes to aging, there are still many unknowns. One thing is clear, pyridoxamine prevents one of the key processes thought to be involved in aging and it also prevents a reaction that leads to the loss of function in our cells, tissues and organs. Glycation prevention was also shown to be a significant help in preventing the complications related to diabetes, a state of rapid AGE/ALE formation.

It has been said that life is the prevalence of the biological over the chemical. Glycation is the perfect example; it is a spontaneous, chemical and detrimental reaction occurring in our body without the control of enzymes. Our body’s response to it is to trap reactive sugar molecules and prevent the permanent glycation of proteins. Pyridoxamine and Benfotiamine feed those reactions and offer protection against tissue damage associated with AGE/ALE formation in the body. They are a useful ally in the treatment and prevention of a wide range of conditions including diabetes, atherosclerosis, renal failure, inflammation and neurodegeneration. Finally and perhaps above all, they lead the way as new anti-aging therapies.

References

21. Ibid.
23. Ibid.

Review.


71 Sadekaa RA, Danilov AV, Vein AM. [Diabetic polyneuropathy treatment by milgamma-100 preparation].


Review.


84 American Health Assistance Foundation, 2005. All rights reserved. 22512 Gateway Center Drive, Clarksburg, Maryland 20871


86 American Health Assistance Foundation, 2005. All rights reserved. 22512 Gateway Center Drive, Clarksburg, Maryland 20871


88 Ibid.


Review.

90 Ibid.


Review.


Lipoic acid is known by a variety of other names. These include alpha-lipoic acid, thioctic acid, 1,2-dithiolane-3-pentanoic acid, 1,2-dithiolane-3-valeric acid, as well as 6,8 thioctic acid. Scientists and health professionals have attempted to categorize it as a glucose optimizer, antioxidant, neurological enhancer, mitochondrial recharger and even an anti-aging remedy. The fact of the matter is that it performs all of these functions to varying but credible degrees. Perhaps this is the reason why lipoic acid is one of the few supplements to slowly and gradually emerge from the fringes of alternative health circles to occupy a solid foothold among health professionals and astute supplement-users alike. Slowly and gradually are operative words here because lipoic acid is the type of nutrient that has demonstrated its worth in a subtly ubiquitous fashion, quietly appearing and reappearing in a variety of crucial metabolic functions.

What Is Lipoic Acid?

Lipoic acid is, biochemically speaking, a sulfur-containing coenzyme which was isolated in 1950 by Dr. Lester Reed of the Department of Chemistry at the University of Texas. From 1950 until the late 1980’s, lipoic acid was studied almost exclusively for its effect on glucose and the cellular mechanism of action that made such an effect possible. Since then, it has come to be categorized under the ever-expanding definition of antioxidant, and the focus of its study has broadened to include these properties. Listed below are the most abundant dietary sources of lipoic acid found in nature:

<table>
<thead>
<tr>
<th>Food</th>
<th>Serving</th>
<th>Lipoic acid/per serving (in micrograms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beef kidney</td>
<td>3 ounces (85g)</td>
<td>32</td>
</tr>
<tr>
<td>Beef heart</td>
<td>3 ounces (85g)</td>
<td>19</td>
</tr>
<tr>
<td>Beef liver</td>
<td>3 ounces (85g)</td>
<td>14</td>
</tr>
<tr>
<td>Spinach</td>
<td>1 cup raw (30g)</td>
<td>5</td>
</tr>
<tr>
<td>Broccoli</td>
<td>1 cup raw (71g)</td>
<td>4</td>
</tr>
<tr>
<td>Tomato</td>
<td>1 medium (123g)</td>
<td>3</td>
</tr>
<tr>
<td>Peas</td>
<td>1 cup raw (145g)</td>
<td>7</td>
</tr>
<tr>
<td>Brussel sprouts</td>
<td>1 cup raw (88g)</td>
<td>3</td>
</tr>
<tr>
<td>Rice bran</td>
<td>1 cup (118g)</td>
<td>11</td>
</tr>
<tr>
<td>Egg yolk</td>
<td>1 large (17g)</td>
<td>0.3</td>
</tr>
</tbody>
</table>

At this point it must be noted that in the majority of human clinical trials, the amount of lipoic acid used is between 200 and 800 milligrams.

What Does Lipoic Acid Do?

The fundamental pillars of lipoic acid’s overall function can arguably be simplified down to two; a glucose metabolizer and an antioxidant. Lipoic acid has also been examined for its ability to generally enhance the mitochondria, to improve neurological function, and to provide an important degree of overall resistance against the aging process. However, these added benefits can effectively be categorized as residual advantages or sub-categories of the two all-encompassing capacities of glucose metabolism and antioxidant activity.

Lipoic acid is generally known for being essential in the oxidation of alpha-keto acids in metabolism, especially pyruvate. It is more specifically regarded as a coenzyme in the oxoglutarate dehydrogenase complex of the citric acid cycle. Furthermore, as nutrients and subsequent micronutrients (including antioxidants) are converted for usage at the cellular level by the mitochondria, supplemental lipoic acid simultaneously becomes converted by the mitochondria to its effective metabolite, dihydrolipoic acid (DHLA).

Lipoic acid is unique among anti-oxidants in that it is both water-soluble and fat-soluble. Like the thiol antioxidant...
glutathione, lipoic acid is part of a redox couple, with lipoic acid itself being the oxidized precursor of the reduced form metabolite known as Dihydrolipoic Acid (DHLA). Dietary sources of lipoic acid, most notably red meat and spinach, are readily converted to DHLA by the pyruvate dehydrogenase enzyme complex (PDH). Unlike glutathione, for which only the reduced form (GSH) is an anti-oxidant, both the oxidized and reduced forms of lipoic acid are anti-oxidants. Lipoic acid is effective against hydroxyl radicals, hypochlorous acid and singlet oxygen, but not against hydrogen peroxide or superoxide. DHLA, on the other hand, is effective against hydroxyl, superoxide, peroxyl reactive oxygen species and hypochlorous acid, but not against hydrogen peroxide or singlet oxygen. From a limited perspective, DHLA’s antioxidant properties are superior to those of lipoic acid. DHLA can regenerate Vitamin C and Vitamin E from their oxidized forms. Furthermore, DHLA (like coenzyme Q10) has two hydrogens to donate in the contention against Reactive Oxygen Species (ROS), thus possessing the ability to neutralize free radicals without becoming one in the process.

What is Lipoic Acid's Overall Mechanism of Action?

Lipoic acid is absorbed from the small intestine and distributed to the liver via the portal circulation and to various tissues in the body via the systemic circulation. It is comprised of two isomers that are also enantiomers. One is R(+) - lipoic acid and the other is S(-) - lipoic acid. Only the natural R(+)- lipoic acid enantiomer is bioactive. The S(-)-lipoic acid enantiomer is purely an artificial creation that only exists as a result of the manufacturing process to create commercial lipoic acid supplements. R(+) - lipoic acid readily crosses the blood-brain barrier and is found, after its distribution to the various body tissues, intracellularly, intramitochondrially and extracelluarly. It has been found to exhibit antioxidant activity in all of these environments, not to mention the aqueous and lipophilic ones.

As previously mentioned, R(+) - lipoic acid is metabolized to its reduced form, dihydrolipoic acid (DHLA), by the pyruvate dehydrogenase enzyme complex (PDH). DHLA forms a redox couple only with the R(+) - lipoic acid enantiomer. It is also metabolized to lipoamide, which functions as the R(+) - lipoic acid cofactor in the multienzyme complexes that catalyze the oxidative decarboxylations of pyruvate and alpha-ketoglutarate.

Exogenous lipoic acid has been shown to increase ATP production and aortic blood flow during reoxygenation after hypoxia in a working heart model. It is thought that this is due to its role in the oxidation of pyruvate and alpha-ketoglutarate in the mitochondria, which enhances energy production. This activity, probably more so than its antioxidant properties, may account for its possible benefit in diabetic polyneuropathy.

R(+) - lipoic acid has been found to decrease urinary isoprostanes, Oxidised LDL Cholesterol (O-LDL) and plasma protein carbonyls - which are all markers of oxidative stress. With regard to R(+) - lipoic acid’s vaunted antioxidant capability, it appears to fundamentally initiate the recycling of other pivotal biologic antioxidants, particularly vitamins E and C, glutathione and coenzyme Q10. Finally, both R(+) - lipoic acid and DHLA are effective in the specific chelation of heavy metals such as zinc, iron and copper.

**PART ONE: R(+) - ENANTIOMER VS S(-) - ENANTIOMER; Why This Distinction is So Important.**

Prior to any discussion about the importance of one enantiomer over another, it is important to explicate the concept of what these enantiomers are based upon. That concept is called chirality, and it is found throughout the natural world. Very simply put, chirality means "handedness" - meaning the existence of left/right opposition. For example, your left hand and right hand are mirror images and therefore "chiral". To fully appreciate the
potency of this metaphor, it is important to emphasize how each of your hands have identical numbers of fingers, thumbs and palms, yet their relative arrangement makes them different in both structure and function. The term Chiral is derived from the Greek name kheir meaning "hand" and apparently was coined by Lord Kelvin in 1904, in his "Baltimore Lectures on Molecular Dynamics and the Wave Theory of Light" in which he stated "I call any geometrical figure, or group of points, chiral, and say it has chirality, if its image in a plane mirror, ideally realized, cannot be brought to coincide with itself." Perhaps a more ideal metaphor can be borrowed from Lord Kelvin himself: try to imagine the physical existence of a mirror image of any object. Although superficially identical, the complete structural arrangements of the two objects would run inversely to each another. As the number of carbons with asymmetry (chirality) increase in a molecule, the number of possible optical isomers (enantiomers) also increases. With one asymmetric carbon, 2 isomers...with two asymmetric carbons, 4 isomers, with three asymmetric carbons, 8 isomers...that is, the number of isomers is $2^n$, where $n =$ number of asymmetric atoms. Every time such a carbon is artificially synthesized, a pair of isomers (or enantiomers) is created - one natural and bioactive, the other artificial and for the most part, relatively inert.

Vitamin E is a popular and excellent example of the importance of chirality. Vitamin E contains three asymmetric carbons allowing for up to eight possible optical isomers (or enantiomers) to be formed (see Holistic International Volume 1 Issue 4). These are the natural "d" forms of alphatocopherol, beta-tocopherol, gamma-tocopherol, and deltatoxopherol, as well as their artificial mirrored counterparts, namely the "dl" versions of the aforementioned tocopherols. The latter form comprises half the vitamin E content of much of the commercially available vitamin E supplements because they are the result of artificially synthesized versions of this vitamin. Natural sources of vitamin E, such as soy, palm or wheat germ oil will contain only the natural, bioactive "d" versions. In the case of vitamin E, however, the synthetic "dl" enantiomers which comprise half of any supplement utilizing artificial sources of this vitamin are not specifically harmful. They are simply not absorbed as well as the "d" enantiomers, in effect "watering down" the vitamin E supplement.

There are other examples where artificial enantiomers can in fact be harmful. One such example is the distinction between the natural cis isomer and the synthetic trans isomer of polyunsaturated fatty acids. When the natural cis isomer is exposed to the heat and pressure of the manufacturing process of hydrogenated vegetable oils, the cis isomer is actually twisted out of its original proportions, creating the artificial trans isomer. The difference between the natural cis isomer and the trans isomer is simply a matter of alternating a point of reference within the respective atomic structures of each fatty acid. The problem, however, is that even such a simple alteration at the molecular level completely alters the effect of the fatty acid in the human body. This phenomenon was aptly demonstrated in a truly massive study involving 80,000 nurses in the United States. The purpose of this study was to determine if the type of fat in a diet was more important than the actual amount of fat with specific regards to heart health. Not only did this study determine the former to be true, but it also found that the natural cis isomer also offered a degree of protection against the risk of Type II diabetes, while the artificial trans isomer actually increases that risk.

Now that we have grasped the macro explanation of why the natural enantiomer is the perfunctory first choice for most molecules, a detailed micro explanation of why it is preferable in the case of lipoic acid is also in order. As mentioned earlier, lipoic acid is converted in the mitochondria into its effective metabolite dihydrolipoic acid (DHLA). The specific enzyme that is actually responsible for this conversion process is called the pyruvate dehydrogenase enzyme complex or PDH. In order for this conversion process to be initiated, PDH must recognize and be stimulated by lipoic acid. Since the PDH is purely endogenous (and therefore natural), it will easily recognize the natural $R(\pm)$- enantiomer and follow suite with the
conversion to dihydrolipoic acid (DHLA). The S(-)-enantiomer on the other hand, being an artificial counterfeit with no real place in nature, will not be so easily recognized by PDH for conversion to DHLA. This is not to say that the ersatz S(-)- enantiomer isn't capable of managing at least some conversion to dihydrolipoic acid, because it does possess enough of a similarity to the R(+)- enantiomer to do just that. However, it cannot do it very well or in quantities anywhere approaching that of the natural R(+)- enantiomer. The fact of the matter is that the rate at which the PDH enzyme can convert the R(+)- enantiomer into DHLA is at least twenty-four times faster than the rate at which it can do the same for the S(-)- form.10

In some types of cells, the PDH enzyme will refuse to accept the S(-)- enantiomer for DHLA conversion altogether. Furthermore, high quantities of the S(-)- enantiomer will actually compromise the ability of the PDH enzyme to convert even the natural R(+)- enantiomer into dihydrolipoic acid (DHLA).11 Pursuant to the S(-)- enantiomer's handicapped ability to recruit the mitochondrial enzyme complex (PDH) for the conversion to DHLA, S(-)- lipoic acid must resort to unorthodox means to manage even its very limited conversion rate. To do this, S(-)- lipoic acid effectively usurps the activity of an enzyme which was never designed for DHLA conversion, and that enzyme is called glutathione reductase. This enzyme is of course essential for the recycling of another critically ubiquitous antioxidant known as glutathione, from its reduced (GSH) form to its oxidized (GSSH) form. If the resources of glutathione reductase are continuously taxed by the limited conversion to DHLA of the S(-)- enantiomer of lipoic acid, then logic dictates that this enzyme’s ability to recycle glutathione will be compromised. Any action that compromises the operation of glutathione is one that ought to be avoided. R(+)- lipoic acid, for its part, imposes no such strains on glutathione reductase and is readily accepted by the PDH mitochondrial enzyme complex to perform the function assigned to it by evolutionary nature - to convert to DHLA and begin its mitochondrial cascade of events.

**Dihydrolipoic Acid (DHLA) Is The Next Logical Step - Or Is It?**

There is a great deal of information and research to suggest that dihydrolipoic acid (DHLA) is in fact the active metabolite of lipoic acid. It therefore stands to reason that if DHLA is the active ingredient of lipoic acid, why not simply isolate it (in supplement form) and then take it in place of lipoic acid? Although simplistic, this is not an unfair question.

The answer is essentially twofold; firstly, there seems to be a fairly clear delineation of duties between R(+)-lipoic acid and dihydrolipoic acid (DHLA). This delineation of duties is based on the fact that R(+)-lipoic acid is effective against singlet oxygen free radicals where DHLA is not, while DHLA can be effective against hydrogen superoxide free radicals where R(+)-lipoic acid is not.12 Right from the beginning, supplemental DHLA in its isolated form automatically negates the ability to quench singlet oxygen free radicals, compromising the spectrum of lipoic acid’s central role as an antioxidant.

**R(+)-lipoic acid is effective against singlet oxygen free radicals where DHLA is not**

Dihydrolipoic acid’s shortcomings are even more glaringly apparent when we consider the other central role of its precursor (R+lipoic acid), namely that of glucose metabolism. This happens as a result of the decarboxylation process that oxidates pyruvate and alpha-ketoglutarate using the NAD+/NADH conversion process as a catalyst. It is the R(+)-enantiomer of lipoic acid that is responsible for modulating this NAD+/NADH conversion process.13 This conversion process is a direct catalyst (and as a result a significant influence) for the conversion of pyruvic acid to lactic acid prior to its oxidation by acetyl-coenzyme A in addition to its subsequent participation in the Krebs cycle.14 The Krebs Cycle is one of the body’s fundamental biological operations for glucose metabolism, and as previously stated, relies heavily on the NAD+/NADH conversion process as a catalyst, a process mediated not by DHLA but by R(+)-lipoic acid.

**The Krebs Cycle**
A further examination of the NAD+/NADH conversion process reveals more shortcomings of supplemental dihydrolipoic acid taken in the absence of its R(+) -lipoic acid precursor. Excess electrons from the NAD+/NADH conversion process are utilized by the pyruvate dehydrogenase mitochondrial enzyme complex (PDH) to convert R(+)-lipoic acid into dihydrolipoic acid (DHLA). Consuming supplemental R(+) -lipoic acid provides the body with more of this molecule than is immediately required for mitochondrial energy production. The result is that more DHLA is synthesized from it, and this 'surplus' dihydrolipoic acid is simply released into the cell and subsequently to the surrounding fluid where it can be systemically utilized for its antioxidant cascade.15 Furthermore, proper and efficient use is being made of the excess electrons by the pyruvate dehydrogenase mitochondrial enzyme complex (PDH) to convert R(+) -lipoic acid into dihydrolipoic acid (DHLA). However, if there is no R(+) -lipoic acid for PDH to convert to DHLA, what happens to the extra electrons from the NAD+/NADH conversion process?

What happens is that these excess electrons are greeted by a PDH mitochondrial enzyme complex that cannot use them, because it is missing the necessary R(+) -lipoic acid it needs to produce DHLA. The end result is that these surplus electrons simply spin out of control and form superoxide radicals from inside the mitochondria itself.16

These electrons that we are speaking of are all a result of the conversion of Nicotinamide Adenine Dinucleotide from its oxidized form (NAD+) to its reduced form, namely NADH. The "H" simply represents a hydrogen atom, itself consisting of one proton and one electron. This extra hydrogen atom is usurped by the PDH mitochondrial enzyme to convert R(+) -lipoic acid into dihydrolipoic acid (DHLA). A concurrent result, however, is an NAD+/NADH ratio that is more favourable to NAD+. This is important for a number of reasons, not the least of which is that NAD+ is the form of Nicotinamide Adenine Dinucleotide that is readily available as an energy source for the mitochondria. Furthermore, improving the ratio of NAD+ to NADH has direct implications in diabetes. This is due to the close association between an unfavourable ratio of NAD+ to NADH and an inhibition of cellular glucose uptake and utilization.38 In fact, such a ratio has been linked not only to diabetes but also to ischemia conditions as well. Furthermore, a low NAD+/NADH ratio also promotes the formation of Reactive Oxygen Species (ROS) and can be traced to a number of other unfavourable metabolic conditions.39

**Glucose metabolism relies heavily on the NAD+/NADH conversion process as a catalyst, a process mediated not by DHLA but by R(+) -lipoic acid**

Then there is the issue of bioavailability. Even R(+) - lipoic acid itself is a very unstable molecule that requires a careful, high-quality approach to manufacturing in order to insure efficacy. Its melting point is a surprisingly low 46-49 degrees Celsius.17 This is an important point to consider when the average human body temperature is approximately 36.5 degrees Celsius. Using these facts as a source of concern for the stability of dihydrolipoic acid as a stand-alone supplement is by no means unwarranted.

## GLUCOSE METABOLISM; Longer is Better

Lipoic acid was first isolated in order to study its effects on glucose metabolism, which is an extraordinary capability for an antioxidant. As a matter of fact, R(+) - lipoic acid’s insulin sensitivity-enhancing capabilities are so potent that it is prescribed as a drug for Type II diabetics in Germany.18 The heart of this potential seems to lie in the ability of R(+) -lipoic acid to increase the cell’s basal glucose uptake capacity.19 This means that R(+) -lipoic acid can open the cells insulin receptors known as transmembrane receptors (belonging to the large class of tyrosine kinase receptors)- even in the absence of insulin! R(+) -lipoic acid therefore increases insulin sensitivity from the cellular surface, which is where the transmembrane receptors are located-and not at the mitochondrial level. (Incidentally, this latter point is yet another reason why DHLA alone, which begins its work at the mitochondrial level, would be void of R(+) -lipoic acid’s glucose metabolism benefits).
One study of 20 type II diabetics found that oral administration of 1,200 mg of lipoic acid for 4 weeks significantly improved measures of glucose metabolism. Another placebo-controlled human study of 72 type II diabetics found that oral lipoic acid at doses of 600 mg/day, 1,200 mg/day or 1,800 mg/day for 4 weeks improved insulin sensitivity by 25%. It is also more than noteworthy to emphasize that all of these studies were conducted using the racemic form of lipoic acid, 50% of which is composed of the artificial S(-)- enantiomer. Insofar as insulin sensitivity is concerned, this ersatz lipoic acid twin (depending on which cell is examined) is either only partially effective or not effective at all. Increased insulin resistance (or inversely, decreased insulin sensitivity) develops to some degree in most people in a manner concurrent with the aging process. R(+)- lipoic acid’s glucose-dispersing abilities are therefore one of the reasons why it has become almost standard-issue in any anti-aging regimen.

However, in order for type II diabetics to seriously consider R(+)-lipoic acid as a possible alternative to traditional forms of treatment, it must offer sustained relief over significant periods of time. This would allow these people the freedom to fulfill their daily responsibilities at work or school, etc, as unencumbered as possible by the constant need for self-medication. One of the current limitations of R(+)-lipoic acid is the speed at which it is absorbed by the bloodstream. The plasma half-life of R(+)-lipoic acid is generally considered to be around 22 minutes. In fact, studies have shown that R(+)-lipoic acid is not only rapidly and completely absorbed into the bloodstream between 30 minutes to an hour after ingestion, but that its peak plasma levels decline equally sharply, dropping 50% within thirty minutes of reaching that peak.

Not only does this not bode well for type II diabetics, but it also spells inconvenience for anyone looking at R(+)-lipoic acid as an alternative (or adjunct) to standard pharmaceutical treatments for metabolic syndrome, or Syndrome X. By some estimates, the latter may affect as much as 25% of the North American population. Insulin resistance is the most significant common denominator between the two conditions, and Syndrome X is a medically expedient term defined by the American Heart Association as "a multiplex risk factor for cardiovascular disease". The spectrum of conditions encompassed by this definition is as follows:

- Abdominal obesity
- Atherogenic dyslipidemia
- Raised blood pressure
- Insulin resistance ± glucose intolerance
- Proinflammatory state
- Prothrombotic state

There is obviously a great deal of overlap between these conditions, none more so than with insulin resistance.

As potent as R(+)-lipoic acid is for increasing insulin sensitivity, its short plasma half-life is an Achilles heel that needs to be addressed. The good news for diabetics is that it is being addressed, and the results have produced several lipoic acid formulations with various excipients or delivery systems that prolong the enhanced sensitivity of the insulin receptors.

The human trials involving these formulations have demonstrated a dramatic and sustained lowering of blood glucose levels. One such formulation was composed of 300 milligrams of racemic lipoic acid in an excipient base of calcium phosphate, starch, cellulose ethers polycarboxylic acid, and magnesium stearate. These tablets were administered to a group of eight type II diabetic patients.
whose ages ranged from 45 to 82, with each patient given 2 such tablets in the morning before breakfast and one more 6 to 8 hours later. The average glucose level of these patients prior to the administration of the controlled release racemic acid formulation was 176.5 mg/dl. After the treatment, that average glucose level dropped to 128.5 mg/dl, an average decrease of 48 mg/dl or just over 27%. A follow-up study using the same formulation and procedure among three more type II diabetic patients produced even more impressive results. Their average blood glucose level dropped from 342 mg/dl to 158 mg/dl, an average decrease of 184 mg/dl or just over 46%.

Their average blood glucose level dropped from 342 mg/dl to 158 mg/dl, an average decrease of 184 mg/dl or just over 46%. It must be noted that these studies were conducted under the auspices of the corporation securing the patent for controlled release lipoic acid. However, there have been more objective, independent studies conducted as well. One of the most encompassing of these was conducted at the Northern California Diabetes Institute at the Seton Medical Center in Dale City, California. Its intentions were two-fold: to determine the pharmacokinetics of a controlled-release lipoic acid supplement and then to determine its safety, tolerability, and effectiveness in patients with type 2 diabetes.

The first part of the study involved 12 human subjects of average health receiving either a single 600 milligram dose of controlled release lipoic acid or a single dose of conventional lipoic acid of the same potency. The plasma profile of lipoic acid was determined 24 hours after the administration of the doses to each group, and pharmacokinetic analyses were then performed. The time to maximal plasma concentration (of lipoic acid) was measured for each group, and the controlled release lipoic acid group measured 1.25 hours (on average) to reach maximal plasma concentration. This was approximately 2.5 times longer than the time required for the conventional lipoic acid to reach maximal plasma concentration.

For the second part of the study examining safety, tolerability and efficacy for diabetics, 21 patients with type 2 diabetes were given 900 mg of controlled-release lipoic acid daily for 6 weeks, followed by 1,200 mg of controlled-release lipoic daily for an additional 6 weeks. Active treatment was followed by a 3-week washout period. Throughout the study, patients continued to take their prestudy antidiabetic medications, which included metformin (Glucophage†), sulfonylureas (Amaryl®, glyburide, and Glucotrol†), acarbose (Precose†), troglitazone (Rezulin®), and insulin (either as monotherapy or in combination). Controlled release lipoic acid was evaluated for safety and tolerability as well as for effects on glycemic control. There were no appreciable side effects or changes in either liver or kidney function or hematologic profiles noted after the administration of the controlled-release lipoic acid. Furthermore, in 15 of the 21 type II diabetes patients, plasma fructosamine levels were reduced from an average of 313 micromoles per litre of plasma to an average of 283 micromol/L after 12 weeks of treatment with controlled-release lipoic acid.

This demonstrates the capability of lipoic acid (or more accurately R(+-)-lipoic acid) to be an effective adjunct to conventional type II diabetes medication as well as a possible alternative on its own, which was itself demonstrated in the previously-mentioned patent application studies.

ANTIOXIDANT ACTIVITY; The Centerpiece Can Now Play Longer

The importance of R(+-)-lipoic acid as an antioxidant requires no further elaboration here. However, it is definitely worth noting that just as the prolonged effects of R(+-)-lipoic acid’s glucose metabolizing properties can benefit diabetics, the prolonged effects of its antioxidant potential can benefit everyone.
The body's intake and production of free radicals is obviously a ceaseless, lifelong process, comparable to (and partly dependent on) methylation in its frequency. This means that under optimal circumstances, the body would require constant protection from an antioxidant as critical as R(+)-lipoic acid. However, we are all too familiar by now with R(+)-lipoic acid's notoriously short plasma half-life. In fact, conventional lipoic acid supplements are almost entirely flushed out of the body within three hours of taking them.  

So unless we consume additional R(+)-lipoic acid capsules every three hours, we are only protecting ourselves for a small part of the day. The importance of continuous protection was demonstrated by an experiment in which racemic lipoic acid was administered to laboratory rodents in large, single-serving, daily dosages. The scientists then subjected them to an artificially-induced "stroke" by cutting off their blood supplies. When the animals received their lipoic acid two hours before their blood supplies were interrupted, it provided them with a measure of protection from significant brain cell death. This protection was not seen in the laboratory animals not administered with the supplement. However, lipoic acid failed to offer any significant neural protection if it was administered either four or six hours prior to the artificially-induced "strokes".

Conventional lipoic acid supplements are almost entirely flushed out of the body within three hours of taking them. The aforementioned experiment is testimony not only to R(+)-lipoic acid's legendary capacity as an antioxidant, but also for the additional protection it provides through its ability to chelate heavy metals such as iron, copper, and cadmium, which can turn relatively 'mild' free radicals into more insidious ones. It is this metal chelating facet of the antioxidant cascade that is most directly associated with R(+)-lipoic acid's lesser known ability to protect brain and nerve cells. As we have seen, the importance of the consistency of that protection is difficult to understate.

References

1 General Pharmacology 29(3):315-331 (1997)
12 General Pharmacology 29(3):315-331 (1997)
14 Ibid.
17 Changshu Fushilai Medicine & Chemical Co.,Ltd. Copyright©2003. All Rights Reserved.
25 US Census Bureau, International Data Base, 2004
26 Ibid.
28 Ibid.
30 Ibid.
31 Ibid.
32 Ibid.
35 Ibid.
I have type II diabetes, which supplement is best for me? From what I understand, my immediate family is also at a risk of developing diabetes. What can they do?

It is true that there is a strong genetic predisposition to the development of diabetes and having a diabetic as a family member is a clear indication that extra attention must be paid to dietary and lifestyle habits. It is a great reason to do what we should all be doing anyways: exercise, eat reasonable portions, watch your weight, eat lots of vegetables, avoid refined grains and sugars and stay away from trans and saturated fats.

Type II diabetes develops slowly and is characterized by a progressively worsening insulin sensitivity that is compensated by an increased pancreatic production of insulin. Blood glucose levels rise uncontrollably once the pancreas is unable to produce enough insulin to offset the cellular insulin resistance (see figure 1).

There are several nutrients that are beneficial to maintain insulin sensitivity and to prevent diabetes. Supplementation can also effectively reverse elevations in blood glucose levels. There are several different approaches possible: (see table 1)

- The prevention of complex carbohydrate digestion which reduces glucose absorption
- Increasing insulin production by the pancreas
- Improving insulin sensitivity
- Preventing postprandial (after meals) hyperglycemia by slowing down the absorption of carbohydrates
- Reducing the occurrence of diabetic complications by preventing protein glycation
- Promoting satiety and weight control

The end results sought are always the same - the reduction of blood glucose levels. The most effective supplements for this purpose will differ from individual to individual. For some, improving insulin sensitivity through supplementation with R(+) lipoic acid will be sufficient to normalize blood glucose levels. For others, a combination approach will be necessary.

The good news is that blood sugar levels can easily be monitored and the effect of supplementation can be observed closely. Monitoring symptoms such as sugar cravings will also help decipher which supplement works best.

For those whose blood glucose levels are normal but who have a family history of type II diabetes, nutrients that improve insulin sensitivity will be best suited. After all, it is the breakdown in the cellular ability to use insulin that leads to type II diabetes.

For type I diabetics who are unable to produce enough insulin to regulate blood sugar levels, supplementation should focus on increasing insulin production by the pancreas and minimizing the consequences associated with the condition.

Protein glycation is a problem for all of us and contributes to the aging process. Glycation and AGE formation have been linked to degenerative conditions such as arthritis, heart disease and neurological diseases. Supplementation with nutrients that prevent AGE formation is beneficial for everyone.
References