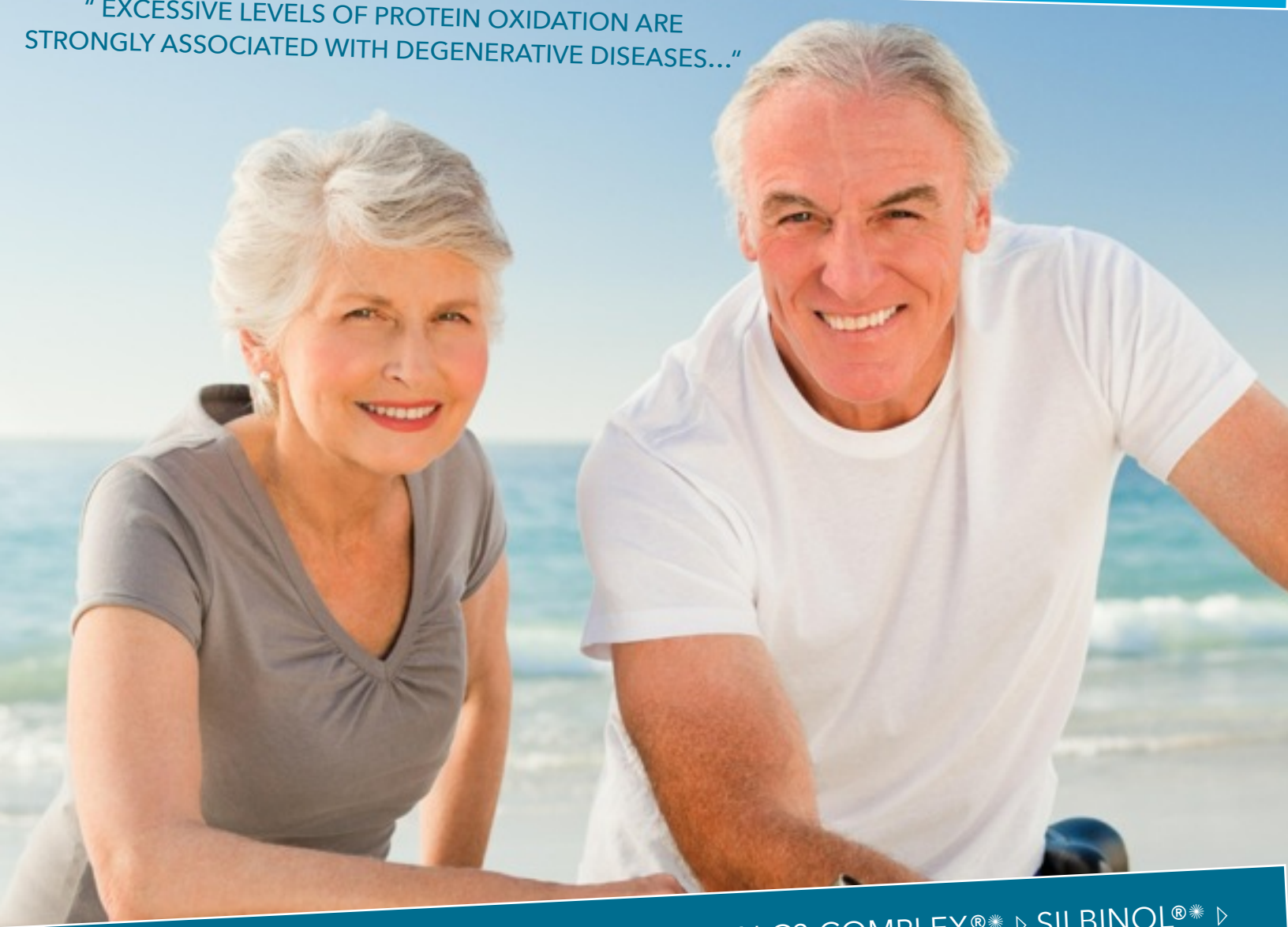
DANGERS OF *PROTEIN OXIDATION*

" EXCESSIVE LEVELS OF PROTEIN OXIDATION ARE STRONGLY ASSOCIATED WITH DEGENERATIVE DISEASES..."



SABERRY®* ▷ SELENIUM SELECT®* ▷ CURCUMIN C3 COMPLEX®* ▷ SILBINOL®* ▷ ROSEMARY ▷ GRAPE SEED EXTRACT ▷ GREEN TEA

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Every minute

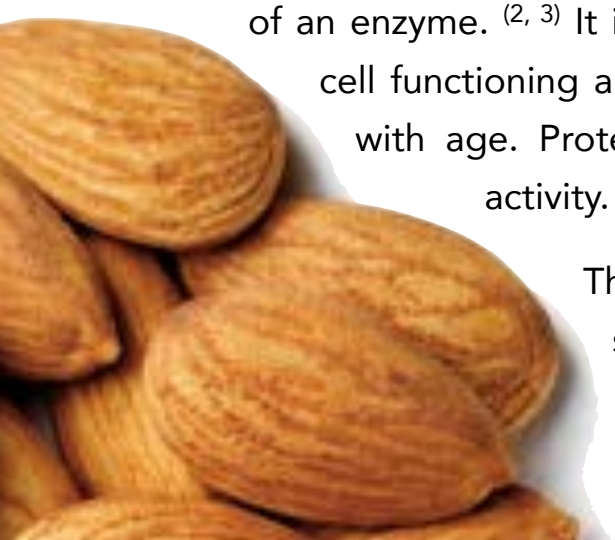
of the day...

a silent, destructive process is occurring throughout your body known as protein oxidation. As we age, this process accelerates and eventually creates the underlying conditions that result in a host of degenerative diseases ranging from cancer and heart disease to diabetes. Understanding this condition and what you can do to modify its lethal reach will go a long way in reducing your exposure to the diseases of aging.

Protein oxidation is caused by free radicals and their toxic by-products attaching to the proteins that make up your body from your cell's DNA, to muscle and organ proteins, brain proteins and artery proteins. [1, 2] It causes lethal mutations to DNA and damage to enzymes and other critical molecules that are essential to normal cell function. [1, 2, 3]

The oxidation of your body's proteins is now an accepted measure of a dangerous condition called oxidative stress, where free radicals are produced in excessive amounts beyond the bodys' ability to neutralize them. [4]

The iron and copper-containing enzymes in our body produce the deadly hydroxyl radical from the always-present hydrogen peroxide in our cells. Hydroxyl radicals are so potent and short-lived that they immediately react with the first proteins at the center of an enzyme. [2, 3] It is well known that enzyme activity is crucial for normal cell functioning and that enzymes become less active or totally inactive with age. Protein oxidation explains this hazardous loss of enzyme activity. [5]



The oxidative damage to our DNA, our cells' memory storage molecule that is copied during every cell division, is caused by protein oxidation and its deadly byproducts.

When our DNA

is damaged or...

mutated by protein oxidation, the dividing cells pass along the DNA mutations to new cells. These mutations accumulate as we age and are a major driving force in cancer development, aging and degenerative diseases. [6, 7]

Higher than normal protein oxidation levels are associated with a large number of human diseases including cardiovascular disease, cancer, Alzheimer's disease, Parkinson's disease, ulcerative colitis and diabetic complications. Emphasis is now being placed on measuring markers of protein oxidation to identify persons who have abnormally high levels of protein oxidation in their blood and serum.

The oxidation of HDL cholesterol is a form of protein oxidation which reduces the ability of HDL (good cholesterol) particles to transport cholesterol away from the arteries. Patients with established cardiovascular disease have higher levels of oxidized HDL in their blood than cardiovascular disease-free subjects. Furthermore, human atherosclerotic lesions have been found to contain elevated levels of oxidized HDL. [8]

LDL cholesterol carries cholesterol to the arteries and is often referred to as the 'bad cholesterol'. Oxidized LDL cholesterol (OXY-LDL), another form of protein oxidation, is a biomarker for diagnosing patients who have already-existing coronary artery disease. Levels of oxidized LDL cholesterol are also being used to determine a persons' risk of developing coronary artery disease rather than simply measuring their total cholesterol. Not only the level of oxidized LDL, but the ratios of oxidized LDL to total cholesterol more accurately identifies patients who have coronary artery disease versus healthy patients. [9]

Protein carbonyl levels, a key protein oxidation biomarker, are now being applied to measure a person's risk of developing certain cancers.

One study revealed

that protein carbonyl levels...

are higher in breast nipple fluids taken from women diagnosed with breast cancer than in breast fluids taken from healthy women. The study also showed that protein carbonyl levels in breast fluids are higher in pre-malignant women and will help identify women who are at greater risk of developing breast cancer. [10]

Protein carbonyl levels in the blood of patients with chronic lymphocytic leukemia and chronic myeloid leukemia are employed as a marker for both the diagnosis and progression of these diseases. Other oxidation markers, such as TBARS and MDA (cell membrane damage measurements) are identified along with protein carbonyl levels in some studies. [11, 12, 13]

Dangerously high protein carbonyl levels are found in the serum of children with malignant tumors [14], patients with active ulcerative colitis [15], diabetic patients with advanced chronic kidney disease [16] and lung cancer patients. [17]

Oxidized brain protein levels are now an accepted measure of the development of Alzheimer's disease, starting with mild cognitive impairment to early and late-stage Alzheimer's progression. [18] Nitrated brain proteins are another dangerous form of protein oxidation associated with cognitive diseases. Higher levels of protein nitration have been identified in patients with all degrees of dementia, including full-blown Alzheimer's disease. [19] Following protein oxidation biomarkers, such as protein nitration, holds promise for early diagnosis, progression and treatment of these diseases. [18, 19]

Higher levels of protein oxidative damage are found in the plasma of type 2 diabetics compared to healthy controls, and data suggests that reduced free radical scavenging in the plasma of diabetics makes them more susceptible to protein oxidation. The greatest difference seen in diabetics vs. non-diabetics is that diabetics have higher serum levels of advanced oxidation protein products (AOPP). This form of severe protein oxidation is higher in long-term diabetics (ten years or more), non-diabetic obese patients and in patients with blood lipid disorders. [20, 21, 22] Diabetic patients who have poor glycemic control have higher serum levels of protein carbonyls and advanced oxidation protein products than diabetics who have good glycemic control. [23]

Supplementation with

antioxidants and other...

dietary ingredients have clearly been shown to lower oxidized protein levels in cell studies and human clinical trials.

Sabinsa's Saberry® brand of amla extract is a broad-spectrum antioxidant which quenches peroxynitrite, superoxide, and hydroxyl radical in both water-soluble and fat-soluble systems using the ORAC (oxygen radical absorbance capacity) tests. These tests were developed mainly to compare the antioxidant potency of natural plant extracts, fruits and vegetables compared to a well-known vitamin E derivative, Trolox, so that fair antioxidant comparisons could be made.

ORAC VALUES OF SABERRY®

ORAC *(H-ORAC) (µmol TE/100g)*	ORAC *(L-ORAC) (µmol TE/100g)*	ORAC *(H-ORAC + L-ORAC) (µmol TE/100g)*	HORAC *(µmol CAE/ 100g)*	NORAC *(µmol TE/ 100g)*	SORAC *(SOD) (KunitsSOD eg/100G)*	SOAC *(µmol VitE/100g)*
267,800	400	268,200	34,500	90,400	10,200	135,100

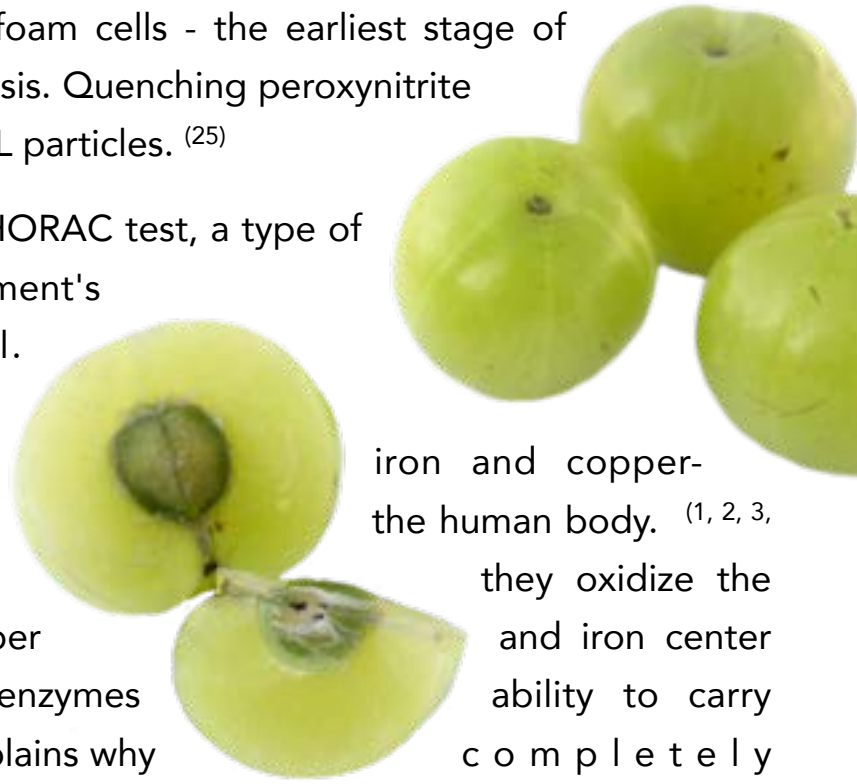
Broad-spectrum antioxidant activity is based on the values of $ORAC_{Total}$ [hydrophilic (H-ORAC) and lipophilic (L-ORAC)- Peroxyl Radical Absorbance Capacity)], HORAC (Hydroxyl Radical Absorbance Capacity). NORAC (Peroxynitrite Radical Absorbance Capacity), SOAC (Singlet Oxygen Absorbance Capacity), and SOD (superoxide dismutase equivalent activity, corresponding to Superoxide Radical Absorbance Capacity).

Saberry® is a leader among water soluble phytonutrients in terms of broad spectrum antioxidant activity, showing a combined ORAC value of 358,600 µmol TE/100g* ($ORAC_{Total}$ + NORAC), HORAC of 34,500 µmol CAE/100g*, SOD capacity of 10,200 kunits SOD eq/100g and SOAC value of 135,100 µmol VitE/100g*.

Sabinsa's Saberry extract scores high in quenching, or neutralizing, peroxynitrite radical, which has been strongly implicated in cardiovascular diseases. [24] Peroxynitrite oxidizes the amino acid tryptophan and sulfur amino acids in the LDL particle. [25]

* TE/g: Trolox Equivalent/100g, VitE/g: alpha- tocopherol Equivalent/100g, CAE/g: Caffeic Acid Equivalent/100g

LDL cholesterol particles deliver cholesterol to the arteries to repair damaged cell membranes, but oxidized LDL particles are no longer recognized by the docking spaces, or the receptor sites, on artery cells. The oxidized LDL particles, however, are recognized by the immune responder cells, the macrophages, and they bond to the damaged LDL particle, forming foam cells - the earliest stage of hardening of the arteries, or atherosclerosis. Quenching peroxynitrite radical blocks its ability to oxidize the LDL particles. [25]



Saberry extract also scores high on the HORAC test, a type of ORAC test that measures a supplement's ability to quench hydroxyl radical. Hydroxyl radical is a powerful damaging free radical that is generated by the iron and copper-containing enzymes found throughout the human body. [1, 2, 3, 26] Hydroxyl radicals are so reactive that they oxidize the amino acids directly adjacent to the copper and iron center of the enzymes and destroys these enzymes ability to carry out their daily functions. [1, 2, 3, 26] This explains why completely inactive or partly inactive enzymes are found in increasing amounts in older people and animals. This form of protein oxidation is one of the driving forces behind the aging process and was first described by Earl Stadtman in 1991. [3, 26]

Saberry's high HORAC score indicates that it is useful at quenching hydroxyl radical, which would indicate that it is useful in healthy aging support.

Saberry®
Multifaceted Antioxidant

Supplementation with selenium has been shown to lower the risks of cancers and other diseases in humans for over a decade, but the exact mechanisms of selenium's anti-cancer effects have been unknown until very recently. [27, 28, 29] The potent effects of selenium can be explained by a lessening of DNA damage, the removal of oxidation products from proteins and the enhancement of DNA repair. Studies demonstrate that selenium acts as a catalyst of protein oxidation repair without being depleted in the process. [27, 28]

Sabinsa's Selenium SeLECT brand of selenomethionine was tested in a study conducted by Vanderbilt University Medical Center and it was found that Selenium SeLECT, is twice as bioavailable as an inorganic form of selenium – sodium selenite. [29] The study involved 120 subjects with an average selenium intake of 10 micrograms per day, well below the recommended dietary allowance of 55 micrograms per day. Participants were given supplemental selenium in either the form of sodium selenite or SeleniumSeLECT. The amount of selenium in both forms needed to optimize nutrient levels in the blood was determined. As compared to sodium selenite, less than half the amount of selenium as SeleniumSeLECT was needed to reach optimal blood levels of selenium. [29]

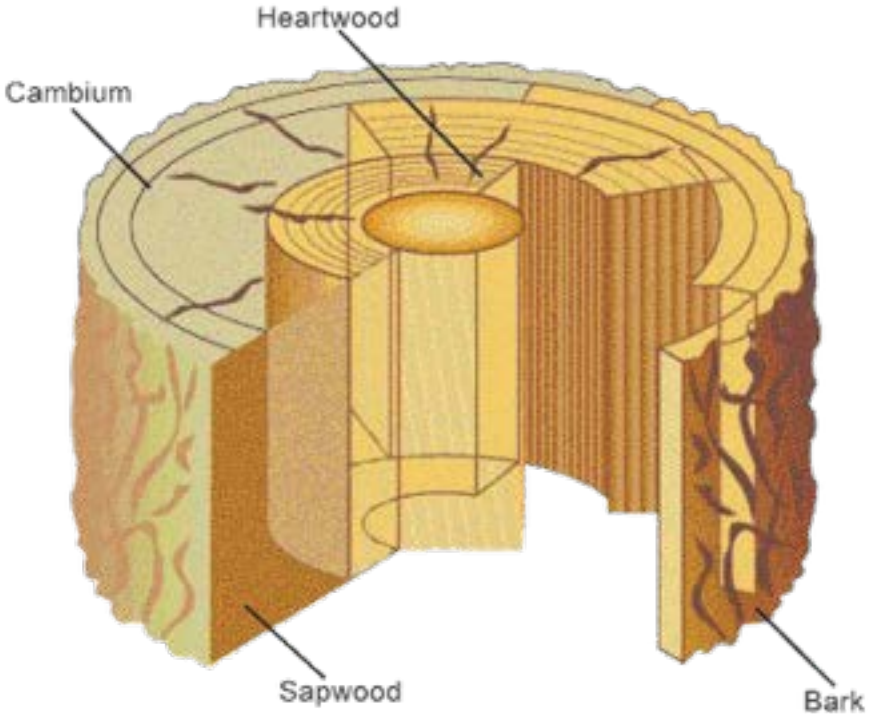
Selenium SeLECT®

Curcumin, the active ingredient in turmeric, is currently undergoing human intervention trials ranging from Alzheimer's disease to cancers. (30) It inhibits protein carbonyl formation and protein nitration in both human blood plasma and blood platelets caused by peroxynitrite radical. Curcumin reduced blood platelet protein carbonyl formation by 40% at the higher doses tested. Lower doses of curcumin were more effective at protecting blood plasma proteins from oxidation. [31]

One study showed that curcumin prevented the oxidation of LDL cholesterol in human blood plasma when exposed to the powerful oxidizing effects of copper sulfate. [32] Copper, always present in human blood, is a major source of LDL cholesterol oxidation. The authors of the study concluded that "Curcumin supplementation could be an effective strategy in preventing LDL oxidation and its impact on atherosclerosis and lesion formation."[32]

Silbinol® from the heart wood of Pterocarpus marsupium is a rich source of Pterostilbene. Pterostilbene, a structural analog of resveratrol, is more stable in vivo than resveratrol. It is known to offer antioxidant and anti-inflammatory support. The antioxidant activities of trans-resveratrol, pterostilbene and quercetin, and the effect of their combination were investigated in human erythrocytes in vitro. Quercetin and pterostilbene protected erythrocyte membranes against lipid peroxidation (IC_{50} values 64 ± 8.7 microM and 44.5 ± 7.8 microM, respectively) (Mikstacka et al., 2010). [33]

The antioxidant effect of pterostilbene in rats with induced diabetes has been assessed. Diabetes decreases the activity of superoxide dismutase, catalase, glutathione peroxidase, glutathione-S-transferase and reduced glutathione significantly in liver and kidney tissues. There were significant improvements in activities of these enzymes, after the rats were treated with pterostilbene at a dose of 40 mg/kg for six weeks. The increased levels of lipid peroxidation measured as thiobarbituric acid reactive substances (TBARS) in liver and kidney of diabetic rats were also normalized by treatment with pterostilbene. Chronic treatment of pterostilbene remarkably reduced the pathological changes observed in liver and kidney of diabetic rats. These results substantiate the in vivo antioxidant efficacy of pterostilbene (Satheesh and Pari, 2006). [34]



Rosemary extract from the dried leaves of Rosemary (Rosmarinus officinalis) contains Ursolic acid, Carnosic acid and Rosmarinic Acid. Rosemary extract's unique cascading power revolves around carnosic acid. After this powerful molecule has extracted a free radical, it changes its structure and becomes carnosol. Carnosol also extracts a free radical to become rosmanol. Rosmanol continues the free radical scavenging until galdosol is created and further continues the scavenging process. All of this is accomplished beginning with just one powerful antioxidant molecule. Carnosic acid cascades into a series of antioxidant molecules to provide sustained anti-oxidant benefits. [35]

Strong inhibitory effect of rosemary extract and its major constituents such as carnosic acid, carnosol and rosmanol on lipid oxidation has been observed in vitro by Chen et al. (1992). Its role in quenching free radical species arising from the lipoxygenase pathway of arachidonic metabolism, in effect helps in tumor prevention (Wagner et al., 1987 and Huang M-T et al., 1991). [36, 37]

Grape seed extract lowered postprandial (after meal) oxidative stress in persons eating a meal rich in fats compared to persons who ate identical meals without taking the extract. Hyperlipidemia, or higher blood lipid levels, is a well-studied risk factor for atherosclerosis caused by after-meal spikes of blood fat. This type of oxidative stress is, in part, caused by increased LDL oxidation and was minimized by grape seed extract supplementation. [38]

Green tea consumption is associated with decreased cardiovascular and cancer disease risk. A human trial in healthy volunteers demonstrated that two weeks of drinking green tea inhibited LDL cholesterol oxidation levels in their blood plasma compared to a week of drinking water. The damaging agent causing the LDL oxidation was identified as malondialdehyde (MDA) and that tea drinking lowered their serum MDA-LDL concentrations. The study with healthy volunteers also showed that green tea drinking lowered serum LDL cholesterol oxidation levels and slowed the oxidation time of LDL cholesterol formation in their serum from 67 to 118 minutes. [39]

SUMMARY

Excessive oxidation of our body proteins is dangerous to our health. Our enzymes, DNA and other key proteins vital to proper cell function are all vulnerable to uncontrolled protein oxidation. Excessive levels of protein oxidation are strongly associated with degenerative diseases of aging, cardiovascular diseases, cancers, cognitive impairment, Alzheimer's, and diabetic complications.

"It is **health** that is real **wealth**..."

- Mahatma Gandhi

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About Sabinsa

Sabinsa's mission is to provide alternative and complementary natural products for human nutrition and well being. Over the past 26 years, Sabinsa has brought to market more than 100 standardized botanical extracts, and privately funded clinical studies in conjunction with prestigious institutions in support of these products. With more than 100 full-time scientists conducting ongoing research in India and the United States, Sabinsa and sister company Sami Labs Ltd. continue to develop, patent and manufacture phytonutrients for the world market. All products intended for human consumption are certified Kosher and Halal. For more information, visit www.sabinsa.com and contact us at info@sabinsa.com.

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