

Vitamin Research News

Dedicated to the Scientific Pursuit of Better Health

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A Special Note To Our Customers

Vitamin Research Products will be moving into our new facility during the first week of December.

We apologize for any brief inconvenience in communication or service you may experience during that time. We greatly appreciate your patience during our move.

Please see The President's Desk on page 3 for more information.

Preventing AGEs and Cross-linkages: A Comprehensive Approach

by Ward Dean, M.D., and James South, M.A.

The Cross-linkage Theory of Aging was first proposed by Dr. Johan Bjorksten in 1941. Bjorksten believed that aging was caused by inter- and intramolecular cross-links in proteins, nucleic acids and other vital macromolecules that caused them to gradually "stiffen" and lose their function.

Bjorksten initially searched for enzymes capable of "dissolving" damaging cross-links. But as he grew older, he realized that he didn't have enough years

of life left ahead of him to allow for the identification and isolation of these enzymes.

Consequently, he shifted his line of research to a more immediately solvable approach: using chelating agents to remove toxic heavy metals (especially, aluminum) that were known to be one cause of cross-linking.

He hoped that by eliminating the cross-link-promoting tri-valent (three

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Dietary Supplements Under Imminent Threat

by James South, M.A.

The European Union Food Supplements Directive (FSD) is scheduled to go into effect in August 2005.¹ This EU law will control food supplement sales and manufacturing in the 25 EU countries.

It will allow only certain vitamins and minerals to be sold, typically at potencies only one to three times the RDA (Recommended Daily Allowance), and will outlaw many of the most natural, bioavailable nutrient forms, such as chromium picolinate, mixed tocopherols E and selenomethionine. Entire product categories, such as amino acids, will be outlawed. Under a related *Traditional Medicines Directive*, herbs may be reclassified as drugs, and stringently regulated accordingly. It is estimated that 5,000 products currently sold in England, Ireland, Holland and Sweden will be outlawed.¹

The Health Minister of New Zealand has just recently agreed to turn over regulation of New Zealand's freedom-oriented nutritional supplement market to a new "trans-Tasman" Agency dominated by

Australia, which is extremely anti-supplement. Australia recently removed 1,600 supplement products (80 percent of those available!) from its health food stores. In Australia, under its *Therapeutic Goods Act*, nutritional supplements are regulated more like drugs than food supplements. The managing director of this agency is based in Australia. The agency is incorporated under that country's laws and will have complete power to issue any anti-supplement rules and orders it wishes to govern New Zealand's health food marketplace.²

During the summer of 2003, Canada quietly harmonized its supplement regulations to those of Australia. They have not yet been implemented; implementation will only occur gradually, in order to avoid waking up Canadian supplement users to the threat until after it's too late.³

The MERCOSUR nations of South America (Argentina, Brazil, Paraguay, Uruguay, and soon to include Bolivia and Chile) have recently agreed to harmonize

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Imminent Threat

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their supplement regulations to the EU Food Supplements Directive.⁴ MERCOSUR has been called a “building block toward the Free Trade Area of the Americas (FTAA).”⁵ President Bush, in a 2002 speech, called for the finalizing of the FTAA, comprising 34 countries including the USA, by January 2005.

From November 1 through 5, 2004, the Codex Committee on Nutrition and Foods for Special Dietary Uses is scheduled to meet in Bonn, Germany. Approximately 50 nations will attend. They will be finalizing worldwide standards for nutritional supplements, with final ratification expected to occur in June 2005. The 25 EU nations make up half of the attendees, and Mr. Basil Mathioudakis will head the EU delegation, and be able to vote their 25 votes (one vote per country) as a bloc.⁶ Mr. Mathioudakis was the person chiefly responsible for drafting the EU’s anti-supplement FSD.⁶ It is expected that the EU delegation will be pushing hard to achieve world supplement standards more or less equivalent to the EU Food Supplements Directive.

Our Supplements Next?

You may well be thinking that because we live in the “land of the free,” what has occurred in those poor countries like England, New Zealand and Canada can’t happen here. If you’re legally savvy,

you might even point out that U.S. Statute 19 USC 3512 safeguards our domestic laws (such as DSHEA, the Dietary Supplement Health and Education Act) from outside interference, prohibiting any other government or trade agency from forcing us to conform to standards that conflict with existing U.S. laws. And yet that’s not the whole story.

Codex and the WTO

The Codex Committee that’s rapidly completing its 10-year work of creating world nutrition supplement standards is a part of a larger organization, the Codex Alimentarius (Latin for “food code”). This agency was set up in 1963 under the joint auspices of the United Nations’ World Health Organization and Food and Agricultural Organization.¹

It is charged with creating comprehensive world-wide food standards to maximize the ease and safety of world food trade. It is also supposed to protect consumers. In the mid-1990s, the Codex Alimentarius organization signed an agreement with the World Trade Organization (WTO), by which Codex creates trade standards that the WTO can then use to resolve international trade disputes.⁶ The WTO is the group charged with enforcement of the Global Agreement on Trade and Tariffs (GATT), which the USA signed onto in 1994.

In a letter to Congressman Dan Burton in 2001, Congressmen Ron Paul and Peter DeFazio made the following observations: “While Codex has no direct authority to force Americans to adopt stringent regulations of dietary supplements, we are concerned that the United States may be forced to adopt Codex standards as a result of the United States’ status as a member of the WTO. According to an August 1999 *Report of the Congressional Research Service*, ‘As a member of the WTO, the United States does commit to act in accordance with the rules of the multilateral body. It [the U.S.] is legally obligated to ensure national laws do not conflict with WTO rules.’ If Congress were to refuse to ‘harmonize’ U.S. laws according to strict Codex/WTO guidelines, a WTO ‘dispute resolution panel’ could find that the United States is engaging in unfair trade because of our failure to ‘harmonize’ our regulations with the rest of the world. In any such trade dispute, the scales are tipped in favor of countries using the Codex standards because of WTO rules presuming that a nation who has adopted Codex has not erected an unfair trade barrier.

Therefore, in a dispute with a country that has adopted the Codex standards, it is highly probable that America would lose and be subject to heavy sanctions unless Congress harmonized our laws with the other WTO countries.”⁷

The “heavy sanctions” referred to are billions of dollars in tariffs (import taxes) that WTO would authorize WTO Codex nations to lay on U.S. exports (and not just on supplement exports). This would make U.S. goods overpriced in the world market, and thus hard to sell, possibly leading to U.S. trade losses in the tens or hundreds of billions of dollars. The U.S. Congress would surely cave in under such pressure, repeal DSHEA and adopt the anti-supplement Codex regulations. This is not just speculation. The U.S. Congress has already given in, in past WTO disputes, to avoid crippling trade sanctions.

The Hour is Late ...

Make no mistake about it. There is a worldwide effort to extinguish vitamin freedom all over the world, including (especially) the USA. It is being driven by a consortium of drug companies and power-hungry regulatory bureaucrats (such as the FDA).

In 1997, acting FDA Commissioner Michael A. Friedman stated in a speech before the Senate Labor Committee: “FDA plans to amend its regulations and procedures for consideration of standards adopted by Codex. This action is being taken to provide for the systematic review of Codex standards in order to enhance consumer protection, promote international harmonization, and fulfill the obligations of the United States under international agreements.”⁸ In November 2000, the Transatlantic Business Dialogue (TABD) issued a press release regarding dietary supplements. A working group of the TABD had just agreed to “Encourage the scientific bodies responsible for the evaluation of the safety of total intakes of vitamins and minerals (EU Scientific Committee on Food and U.S. Food and Nutrition Board) to cooperate closely to harmonize setting upper safe levels for vitamins and minerals.”⁹ The press release also stated: “The TABD...seeks...the removal of...differences in the EU and U.S. regulatory systems.”⁹

The TABD has 120 members, mostly pharmaceutical-type vitamin companies. Many U.S. vitamin companies (some that sell in health food stores, but more that sell in grocery stores and pharmacies) are now owned by, or partnered with, pharmaceutical drug companies. The world drug industry wishes to remove con-

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The information in this newsletter is not intended to provide personal medical advice, which should be obtained from a medical professional, and has not been approved by the U.S. FDA.

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sumers' ability to maintain their health or fight disease through nutritional supplements, thereby forcing them back into the much more lucrative toximolecular pharmaceutical drug market. U.S. pharmaceutical drug sales are \$150 billion to \$200 billion yearly, compared to \$18 billion spent on supplements.

...But All is Not Yet Lost

In spite of the fact that the innovative, relatively free U.S. supplement market could begin to disappear as early as 2006, all is not yet lost. There are various actions we can still take.

The Alliance for Natural Health has filed a lawsuit in the European Court of Justice to overturn the Food Supplement Directive on multiple legal grounds. It has been referred to the court on an expedited basis. It is being litigated by a law firm that has already succeeded in overturning other EU directives. If it can be overturned before the Codex regulations are finalized, it will take much of the steam out of the EU Codex delegation's efforts to model final Codex regulations on the EU Food Supplements Directive.

You can help by donating money (even \$5 or \$10 helps) for this costly battle to the Alliance at www.alliance-natural-health.org. Please do it now! The supplements you save may be your own.

Next, please write, call, fax and e-mail your U.S. senators and representatives. Urge your senators to oppose S. 722, the Dietary Supplement Safety Act, and urge your Congressperson to oppose H.R. 3377, the Dietary Supplement Access and Awareness Act. These misnamed bills would hand great new powers to the FDA to treat dietary supplements as drugs, doing away with most of the protection that consumers and the supplement industry gained under DSHEA. Also ask your Senators to oppose S. 1538, the DSHEA Full Implementation and Enforcement Act. This bill would give the FDA \$105 million to use to harass vitamin manufacturers and health food stores under the FDA's biased, anti-supplement interpretation of DSHEA.

Also, let elected officials in Congress know you don't want them to buckle under any future WTO pressure to conform U.S. laws to anti-supplement Codex standards. Please realize that pharmaceutical industry lobbyists donate \$100 million yearly to the re-election campaigns of representatives and senators. Unless they get large numbers of angry, forceful letters, calls, e-mails, etc., they will naturally tend to take the pharmaceutical industry's interests into account before yours.

You must quickly get educated on this fight. The International Advocates for Health Freedom (www.iahf.com) is run by John Hammell. It's a no-nonsense grassroots organization that's been fighting Codex and trying to alert America to the Codex danger since 1996. Sign up for IAHF's free e-mail alerts. IAHF is a one-man operation, but John is a human dynamo, with world-wide contacts fighting Codex, the EU FSD, etc. Please make at least a small donation (even \$5 or \$10 helps) to IAHF at www.iahf.org. John is the most active, best-educated, constantly working opponent of the global war against supplements that I know of.

Also, please contact your U.S. senators and representatives about the Free Trade Area of the Americas, and tell them you want no part of it. The European Union started out as a trade group, and now it's a supranational government, complete with Parliament and Court of Justice, that dictates the laws of all 25 member nations. FTAA is slated to do the same for the USA. Once it begins, it's only a matter of time until a similar bureaucracy will be set up to remake our laws (and do away with our borders) here in America. Visit www.stopthettaa.org to learn more.

Finally, contact your U.S. representatives and senators and tell them to support U.S. Rep. Ron Paul's H.R. 1146, the American Sovereignty Restoration Act. This legislation will make the U.S. Constitution the supreme law of the land again. Currently, Supreme Court rulings from the 20th century have made treaties, such as GATT/WTO/Codex, superior to the United States Constitution and laws, overriding them whenever there's a conflict.

Time is short, folks. If we don't all do the work now—donate a little money, study, spread the word to your family, friends and neighbors, contact your elected representatives—the supplements we now take for granted may be gone within 18 to 36 months. The handwriting is on the wall, although it's not yet written in permanent ink. Let's erase it now, while we still can!

P.S. I will be updating readers in future issues of *Vitamin Research News* on Codex, EU FSD, etc. as further information becomes available.

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The President's Desk

VRP Is On The Move ... Into A New, Expanded Facility

Vitamin Research Products in the next few weeks will mark a major event in its quarter-century history. In early December, we will be moving into our newly constructed, expanded facility here in Carson City, Nevada.

VRP has experienced strong and steady growth since it was founded in Mountain View, California, in 1979. Our operations have been conducted from our current location since I became president in 1991 and moved the company to Nevada.

It has been extremely gratifying over the years to serve and support ever-growing numbers of people worldwide who have embraced VRP's industry-leading commitment to research and education, and made the choice to enjoy healthier lives.

As a result, our vitamin/supplement product line has grown to several hundred science-based, cutting-edge formulas.

The new facility will enable us to enhance our manufacturing processes and take our customer service to an even higher level—a reflection of our unwavering commitment to developing and providing the finest vitamin and supplement formulas on the market.

Your Patience, Please ...

To ensure your order is not delayed by the Thanksgiving holiday or by our relocation preparations, we encourage you to place your November order early, if possible.

We ask also for your extra patience as phones and Internet connections are scheduled to be transferred on December 3. Any disruption to communications with us should be brief.

Thank you for making this important milestone possible. All of us at Vitamin Research Products are excited about our move and look forward to continuing to serve you in the years to come.

Robert Watson
President/CEO

AGEs, Cross-linkages

Continued from front page

points of attachment) aluminum atoms (which he believed displaced divalent [two points of attachment]) calcium atoms, he would reduce one of the major sources of cross-linking, and thereby “buy enough time” to solve the rest of the cross-linkage problem.

This has been explained in greater detail in the series of articles on the *Cross-linkage Theory of Aging* in VRP’s online library at www.vrp.com/library/732412.html, www.vrp.com/library/734012.html, www.vrp.com/library/733847.html, and www.vrp.com/library/732867.html.

Bjorksten ended his active research career in 1991 with one last publication that summarized his progress up to that point. Ironically, at about the time Bjorksten was retiring from his quest to unravel the cross-linkage problem, other scientists were “picking up the baton”—although they approached the problem from a slightly different direction.

Advanced Glycation End Products of Aging (AGEs)

A characteristic of all long-lived proteins in the body is that as they age, they turn brown and become fluorescent (under UV light), become more cross-linked, less soluble, less elastic, and less digestible by enzymes.

In 1965, Dr. H.B. Bensusan first proposed that it was a process known as the

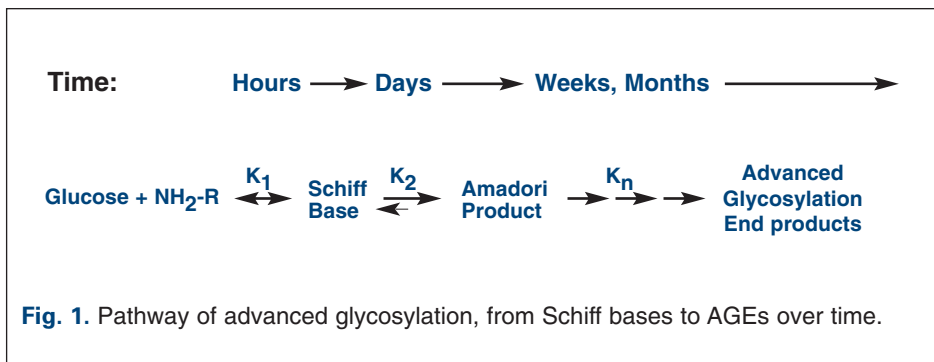


Fig. 1. Pathway of advanced glycosylation, from Schiff bases to AGEs over time.

Maillard reaction that caused these changes. The Maillard reaction is named for the noted French scientist, Louis Camille Maillard (1912), who described the non-enzymatic chemical reactions between proteins and carbohydrates that cause cooked foods to turn brown. This time-honored bit of kitchen chemistry has been used by cooks for centuries to enhance flavor and transform plain foods into delicacies by adding flavor and color to recipes.

In 1985, Monnier, Kohn and Cerami provided further details of the role of the Maillard reaction as a major source of the age-dependent increase in browning, fluorescence and cross-linking of collagen and other tissues.¹ They further developed the idea that it is the Maillard reaction that results in premature aging and degenerative diseases such as diabetes and heart disease. In this regard, many scientists think the human body may be viewed as a “low-temperature oven” with a relatively long—approximately 75-year—“cooking” cycle.²

The Maillard reaction involves a chemical reaction (“condensation”) between a sugar (usually glucose) with a protein. This complex is known as a *Schiff base*. In the human body, this is a reversible reaction, which reaches equilibrium (i.e., stabilizes) within several hours.

With continued exposure to the sugar, the Schiff base undergoes a “rearrangement” known as non-enzymatic glycosylation that results in a more stable, less reversible substance, known as an Amadori product. Again, in the human body, this process reaches equilibrium over several weeks (Fig. 1).

The Amadori product further degrades irreversibly into a number of highly reactive carbonyl (C=O) compounds. These reactive substances, called Advanced Glycation End products have been designated by the acronym AGE.³ AGE is a clever pun which reflects the proposed relationship of these reactive substances to aging and age-related diseases. AGEs can further react with other fats, proteins and nucleic acids to form largely indissoluble cross-links. These AGE products increase with age in many tissues of the body (Fig. 2).⁴

Furthermore, if blood sugar remains elevated for prolonged periods (as occurs in poorly controlled diabetics) that may increase glycation and AGE formation up to four times! This explains why diabetics suffer the premature onset of a wide range of age-related complications including cataracts, retinopathy, neuropathy, nephropathy, atherosclerosis and osteoporosis.^{5,6}

Cross-linkage Theory Gets New Life

Bjorksten was a talented petroleum chemist. Had he been a food chemist instead, he may have appreciated this link between the Maillard Reaction and cross-linking much earlier, and made even greater progress in developing preventive and therapeutic approaches to

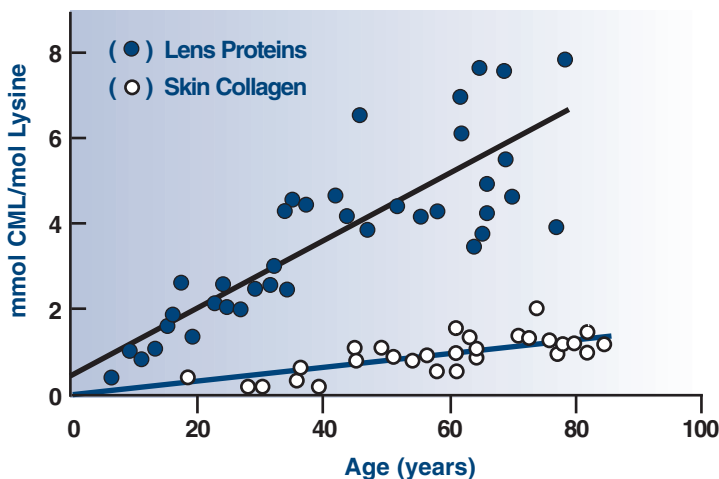


Fig. 2. Increased accumulation of AGEs (CML) with age in human lens protein and skin collagen. (Dyer, et al. The Maillard reaction in vivo, 1991.)

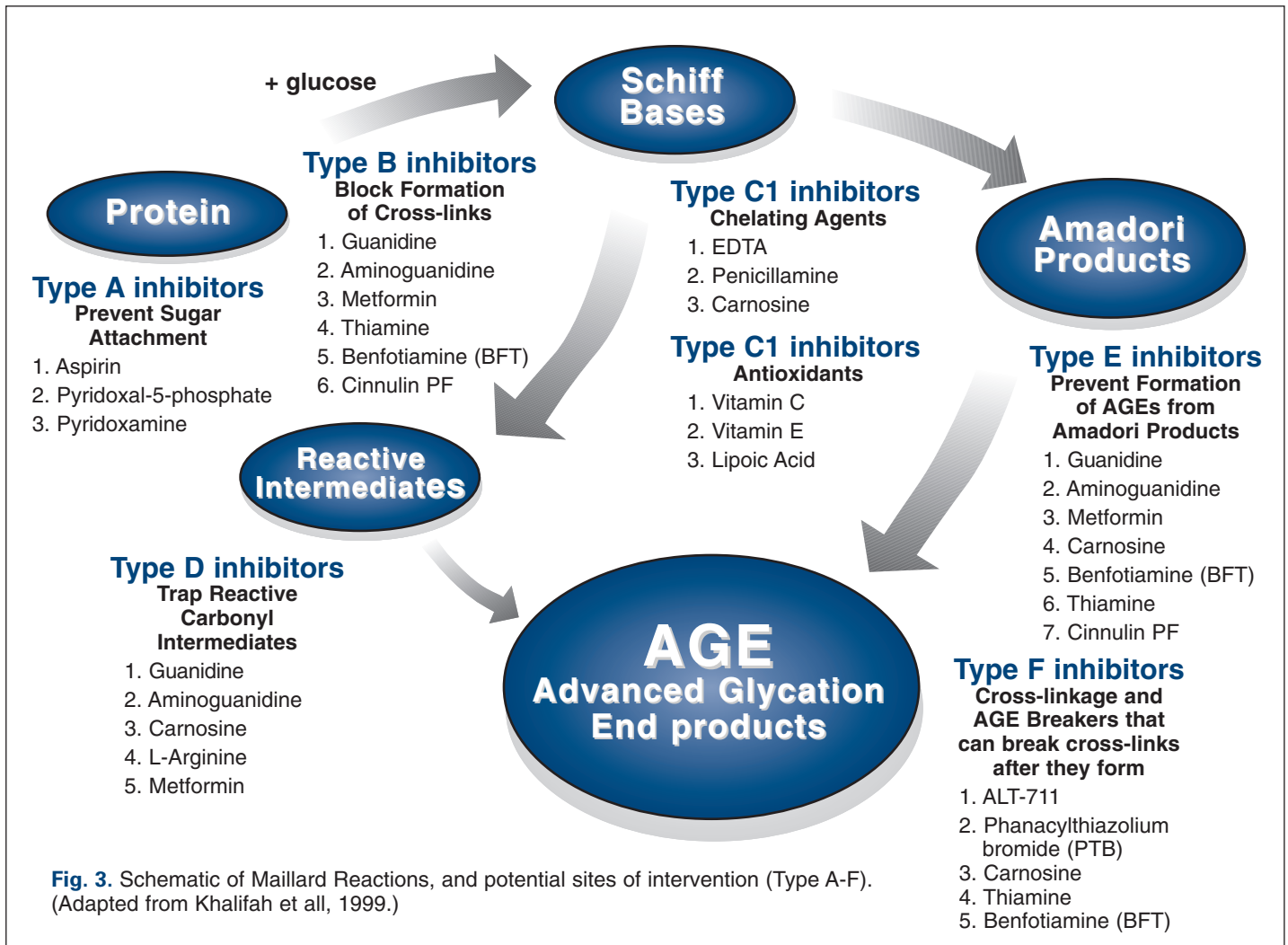


Fig. 3. Schematic of Maillard Reactions, and potential sites of intervention (Type A-F). (Adapted from Khalifah et al, 1999.)

cross-linkage-induced aging. Through their insightful work in understanding this process, scientists like Brownlee, Cerami and Monnier provided renewed impetus and a “rebirth” for the cross-linkage theory.³ Unfortunately, they did this with little attribution to Bjorksten, who had doggedly pursued this approach to aging for more than 50 years.

Cross-linkage Biomarkers: Indicators of Biological Age

An important aspect of any comprehensive theory of aging is the inclusion of techniques (dictated by the theory) that can be used to accurately measure the progress of aging.

Parameters that can be correlated with age and that can be used to evaluate the rate of aging are known as biomarkers.⁷ Scientists have identified a number of unique biomarkers that reflect aging in terms of the Cross-linkage/Glycosylation theory (Table 1).

Continued on page 6

Biomarkers	Effect Being Measured
Pentosidine	Pentosidine is a prominent cross-link in proteins that increases in lens protein and collagen with age.
Carboxymethyllysine (CML)	Carboxymethyllysine (CML) is a major product of glycated proteins, and a general marker of oxidative stress and long-term damage to proteins in aging, atherosclerosis and diabetes.
Glycosylated Albumin	Glycosylated albumin, like hemoglobin, forms cross-links with AGEs in the presence of glucose
Glycosylated Hemoglobin A1c (HbA1c)	Glycosylated Hemoglobin A1c (HbA1c) results from exposure of hemoglobin to glucose, forming an Amadori product.
AGE-Modified Hemoglobin (Hb-AGE)	AGE-modified hemoglobin (Hb-AGE) is an even longer-term indicator of blood glucose control, reflecting the full 60 day half-life of the red blood cell.

Table 1. Biomarkers that reflect aging in terms of the Crosslinkage/Glycosylation theory.

AGEs, Cross-linkages

Continued from page 5

Approaches to Preventing and Removing AGE-Induced Cross-links

Khalifah and his colleagues proposed a schematic of the formation of AGEs, which illustrates a number of specific therapeutic targets (Fig. 3).⁸

Following are some of the most promising substances to use to inhibit/dissolve AGE-induced cross-links.

Goat's rue (Guanidine)

Goat's rue (*Galega officinalis*), or French Lilac, has been used for the treatment of diabetes since medieval times. The glucose and insulin-lowering effects of Goat's rue extract are due to the natural substance, guanidine. We believe Guanidine (Fig. 4) is the herbal prototype for the insulin-sensitizing, glucose-lowering anti-diabetic drug, Metformin (Glucophage), and for the related substance, aminoguanidine. Purified, high-guanidine forms of Goat's rue extract presumably share most of the beneficial effects of aminoguanidine and Metformin, with none of the adverse effects of raw Goat's rue herb.

Metformin (Glucophage)

Metformin is an anti-diabetic biguanide that was derived from the herb Goat's rue (*Galega officinalis*). Biguanide drugs were recognized by Prof. Vladimir Dilman as early as the mid-1970s as the most effective anti-aging drugs in existence. Metformin is known as an insulin receptor sensitizer, capable primarily of lowering blood sugar and insulin.

Dilman also demonstrated that biguanides restored cortisol receptor sen-

sitivity. Metformin has many other beneficial properties, including optimizing lipid profile, reducing body fat, maintaining levels of growth hormone, stimulating immunity, and extending the maximum lifespan of experimental animals.

Dr. Dean reviewed the anti-aging/life-extending effects of Metformin in the November 1998 *Vitamin Research News* (online at www.vrp.com/library/732342.html). Despite its wide range of reported beneficial effects, Metformin has not, to my knowledge, been tested for its ability to retard AGEs and AGE-induced cross-links. However, we assume that AGE-inhibiting effects would be found for Metformin, if anyone bothered to look. This situation is analogous to other similar nutrients that have been tested for specific effects, while overlooking effects attributed to their structural "cousins."

For example, Acetyl-L-Carnitine (ALC) is used primarily for its cognitive-enhancing, mitochondrial membrane normalizing effects, while L-Carnitine is usually used for its cardiovascular, performance-enhancing, and lipid-normalizing benefits.

Dr. Brian Liebovitz, author of the book, *L-Carnitine-Vitamin Bt*, believes, however, that L-Carnitine is equal to or better as a cognitive enhancer than ALC—it is just that no one has ever evaluated the cognitive enhancing effects of L-Carnitine. We think the same could probably be said for idebenone and its close relative, coenzyme Q10. They both probably have very similar actions.

Likewise, we think Metformin and guanidine probably share the AGE and cross-linkage-inhibiting effects of their relative, aminoguanidine. Metformin requires a prescription in the United States.

Aminoguanidine (Pimegedine™)

Aminoguanidine is a substance that has been known for over 100 years. It is

structurally very similar to guanidine, the active ingredient in the herb Goat's rue. Aminoguanidine has aroused a great deal of interest in the last twenty years, due to its demonstrated ability to block the formation of AGEs and AGE-induced cross-linkages in both animal and human clinical studies.

Aminoguanidine inhibits AGE formation, preventing AGE-induced cross-links in collagen and other tissues. Fortunately, aminoguanidine does not interfere with the formation of normal collagen cross-links, which are required for structural integrity. Another mechanism by which aminoguanidine is believed to act is by enhancing the action of nitric oxide (the same mechanism by which Viagra® functions).^{9,10}

Aminoguanidine also reduces the formation of lipofuscin (age pigment) and prevents or reduces cataracts, atherosclerosis, diabetic retinopathy, nephropathy and neuropathy (Fig. 5).^{2,11-13} In a study with rats, scientists occluded the arteries that supply blood to the brain, inducing an "experimental stroke." The scientists administered aminoguanidine in various concentrations and at various time intervals following inducement of the "stroke." They found that the size of the brain damage from the loss of blood flow could be greatly reduced with aminoguanidine, even when administered as much as two hours after the onset of the reduction in blood flow.¹⁴ This indicates that aminoguanidine may also be effective in the prevention and treatment of strokes.

In one study of diabetic patients, after four weeks of therapy with aminoguanidine, LDL cholesterol decreased almost 30 percent, and total cholesterol and triglycerides both decreased almost 20 percent. Hemoglobin-AGE levels—a circulating marker of the degree of glycosylation—also decreased dramatically (13.8 U/mg Hb at the beginning of therapy, to 10.0 U/mg Hb after only four weeks).¹⁵

Although aminoguanidine's effects on blood sugar and insulin have not been examined, to my knowledge, we believe that if such studies are conducted, the effects will be positive. For example, Metformin and Goat's rue (guanidine) are best known and best tested for their beneficial effects on blood sugar and insulin, due to their insulin-receptor sensitizing properties. Aminoguanidine, on the other hand, is best known and best tested for its

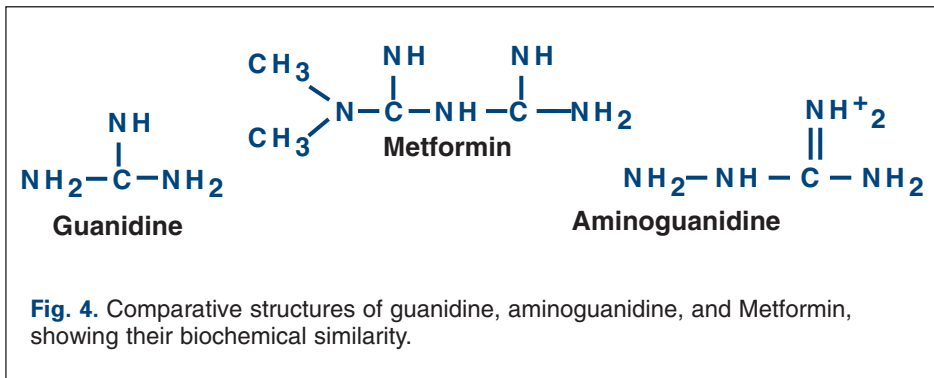


Fig. 4. Comparative structures of guanidine, aminoguanidine, and Metformin, showing their biochemical similarity.

AGE-inhibiting effects. However, we think that if these substances were to be comprehensively evaluated together, we would find that they share most properties, to a greater or lesser degree, due to their closely related structures. Anecdotal reports from patients and physicians appear to confirm this.

Aminoguanidine is very safe, as indicated by short-term human studies which used relatively high doses of 1,200 mg daily.¹⁶ (This is in comparison with a usual human dose of 100 to 300 mg daily). The dose required to cause death in half the animals (mice) to which it was administered (Lethal Dose 50 [LD50]) was 1,800 mg/kg.⁹ That would be equivalent to a human dose of almost 300 gm!

Pyridoxal-5-Phosphate (P5P)

P5P, the active form of vitamin B6, has been found to significantly reduce the nonenzymatic glycosylation (formation of AGEs) of bovine serum albumin (BSA) with radioactive-labeled sugar. Of the substances tested, P5P was exceeded only by aminoguanidine in its ability to inhibit AGE formation (Fig. 6). Combining P5P with guanidine, Metformin, or aminoguanidine may enhance their AGE-inhibiting actions even more.¹⁷

Pyridoxamine

Pyridoxamine (PM) is a third form of B6, and is a well-established inhibitor of AGEs such as CML and CEL (carboxyethyllysine).¹⁸ It has recently been discovered that some AGEs, such as CML, can also be derived from lipid per-

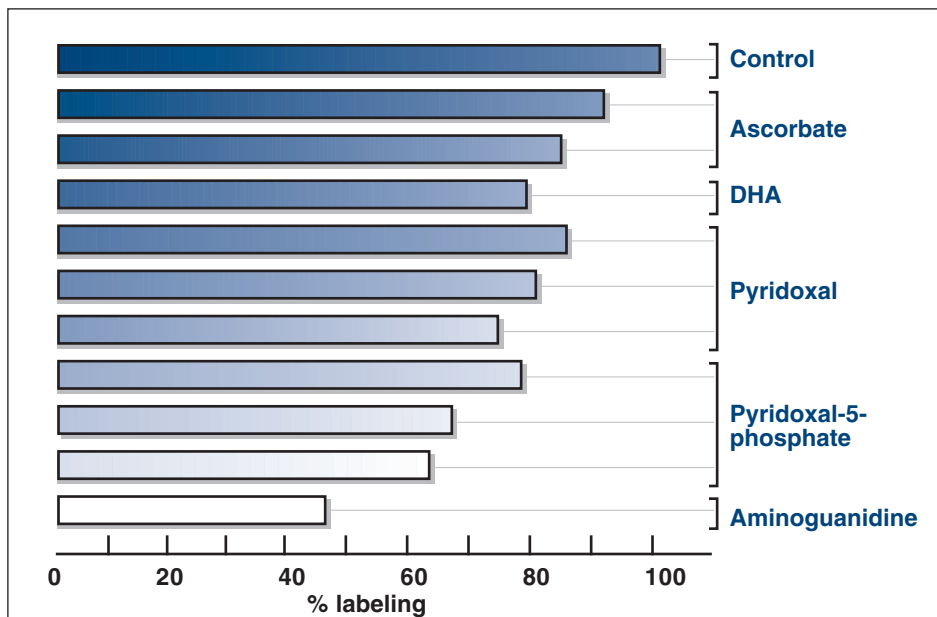


Fig. 6. In vitro (“test tube” test) comparing the formation of AGEs on bovine serum albumin when exposed to glucose. Note the dramatic reduction when aminoguanidine or pyridoxal-5-phosphate are added. (Khatami, et al. *Life Sciences*, 1988)

oxidation (“rancid fat”) products.²⁴ These products are called ALEs (advanced lipoxidation end products). PM has been shown in recent studies to block ALE formation, as well.^{20,21} CML is the predominant AGE in intracellular neurofibrillary deposits in patients with Alzheimer’s disease and in macrophage-derived foam cells in human atherosclerotic plaques. Its concentration in human tissues increases significantly with age.²²

PM has also been shown to block formation of methylglyoxal-AGEs, one of the main AGEs formed inside cells.²³

PM reduces methylglyoxal levels in red blood cells and plasma proteins in diabetic rats and prevents formation of the AGE pentosidine in plasma proteins.²³

ALT 711, Vitamin B1 (Thiamine) and Benfotiamine

Alteon is a pharmaceutical company that is focused on developing drugs to prevent the formation of AGE-induced cross-links, as well as to dissolve cross-links after they are formed. Several of the company’s products are currently undergoing FDA-sanctioned trials.

One of the products, ALT-711, improved arterial elasticity, indicating an ability to “undo” cross-linkages.²⁴ This is the first drug that is specifically designed as a cross-linkage breaker.

Interestingly, ALT-711 is a derivative of thiamine (vitamin B1). In their book *Life Extension*, Durk Pearson and Sandy Shaw reported that thiamine was an effective cross-linkage inhibitor. Durk and Sandy were, at that time, consuming two grams of thiamine each day in their personal anti-aging regimens. Thiamine, the parent compound of ALT-711, may ultimately also prove to be an effective cross-linkage breaker as well as inhibitor.

Benfotiamine (S-benzoylthiamine-O-monophosphate) is a synthetic, fat-soluble form of thiamine (vitamin B1) that

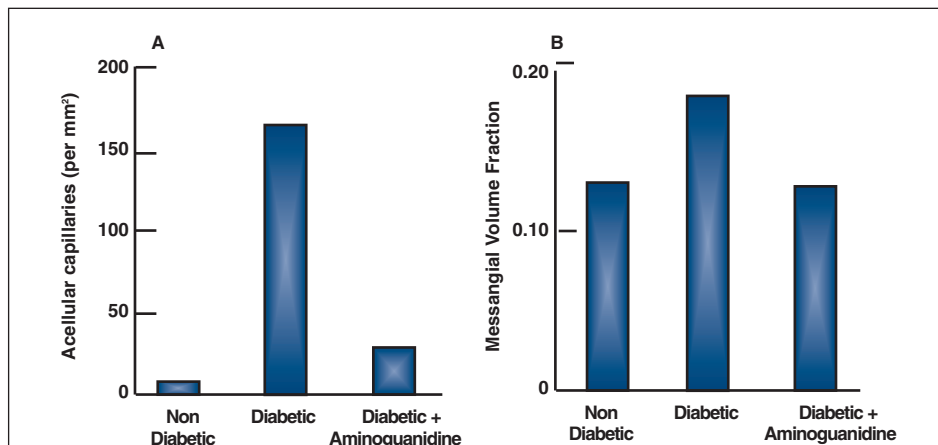
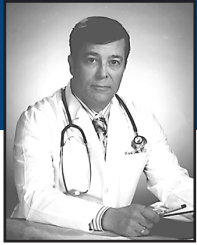


Fig. 5. Effects of aminoguanidine on structural abnormalities of long-term diabetes in retina and glomerulus. Presumably, Metformin and guanidine (Goat’s Rue extract) would have similar effects. (Brownlee, et al. *N. Engl. J Med*, 1988).

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CUSTOMERS' CORNER

by **Ward Dean, MD**
VRP Medical Director

Hyperlipidemia

Dear Dr. Dean,

I am a 72-year-old male. My total cholesterol is 205, HDL 54, LDL 141. I would like to know if any of the products I am taking would drive up my LDL. My meds are Lovastatin 20mg and Pepcid® 20mg. Thank you for your help. — Mr. L.

Dear Mr. L.,

I don't think any of the products you are taking are adversely affecting your LDL. I would add 1,500 mg of *Niacin* or *Inositol Hexanicotinate* (IHN—a non-flushing form of niacin) to your regimen. Please see my articles on niacin on VRP's website (www.vrp.com).

Lovastatin may result in a lowering of your tissue CoQ10 levels. Consequently, I recommend that you increase your dose of *CoQ10* to about 150 mg per day.

Ward Dean, M.D.

Preventive Recommendations

Dear Dr. Dean,

I am healthy, 33 years old, and am not taking any prescription medications. I take *Extend ONE* daily along with two caps of calcium/magnesium. I'm lactose intolerant so I figured a little extra calcium and magnesium would be good.

My overall cholesterol is a little high, around 225, but the HDL/LDL ratio is fine; my doctor doesn't seem concerned about it. My diet is centered around eating simple whole grains, lean meats, lots of fruits and veggies.

I exercise a lot, especially hiking, running, biking and weights, and worry a little about preserving my joint health as I get older (I have a couple of knee/ankle injuries but nothing serious and no surgeries). Would a joint sup-

plement like glucosamine/ chondroitin be worth it as a preventative to osteoarthritis (doesn't appear to be any studies on this) and to maintain overall joint health?

And, do you have any other recommendations for supplements to add as a health maintenance and preventive/life-extension regimen? I guess what I'm asking is what would you take if you were me? — Mr. Y.

Dear Mr. Y.,

I agree that a good joint formula would probably help you to maintain your joint health. Naturally, I suggest *Nutri-Joint*. Although there are no studies that prove its preventive benefits, there are studies that show that formulas like *Nutri-Joint* increase joint space (i.e., the space between bones).

You asked what I would take if I were you. I'd start by working up to *Optimum 6*, as well as the *Nutri-Joint*.

Also, considering the modest supplement regimen that you are on now, and your desire to optimize your life-extension program, I would add *AGEBlock™* and/or VRP's new *Benfotiamine/Pyridoxamine AGE Inhibitor*.

Ward Dean, M.D.

Red Clover Extract and Prostate

Dear Dr. Dean,

I've been using your *Beta-Sitosterol* for enlarged prostate. It seems to be very helpful. I have tried many of the saw palmetto formulas in the past, but they all seemed to increase my symptoms. My urologist has suggested trying red clover.

I wonder if it would be okay to use the red clover with the *Beta-Sitosterol*? I would appreciate your opinion on this. Thank you. — Mr. H.

Dear Mr. H.,

I agree that there are some data—both in vitro and limited human clinical studies—that indicate that red clover extract may indeed be beneficial in normalizing abnormal prostate tissue.

Although I think the studies with beta-sitosterol, pygeum extract, saw palmetto, and stinging nettle extract—the ingredients in VRP's *ProstaCol®*—are more conclusive than those with red clover extract, it is possible that you may obtain additional benefit by adding *Red Clover Extract* to your current regimen, as your physician suggested.

Ward Dean, M.D.

Chronic Low Back Pain, Sciatica

Dear Dr. Dean,

I am 38 years old. I have had chronic back pain for many years and have nerve and disc damage in L3, 4, 5 and S1. I get numbness running down my left leg. My doctor at the VA hospital has me on an anti-arthritis drug, which I do not take much because it makes it harder for my blood to coagulate.

I was taking ibuprofen (800 mg). I stay as active as I can. I get an epidural of cortisone in my tailbone area every three months.

I also take *Vicodin®* when the pain gets really bad and I can barely walk without my cane. I am not looking for any miracles, just a breakthrough. What do you suggest? Thank you for your time and any help. — Mr. T.

Dear Mr. T.,

Basically, everything you are doing is merely treating the pain—nothing is helping to alleviate the cause. Here are some suggestions:

First, try a combination of *Nutri-Joint*, *Strontium* and *Essential Minerals*. These will not give instant relief, of course, but may help to increase formation of cartilage and improve bone density. Over time, this may provide some

relief of the nerve root pressure and irritation that is causing your symptoms.

Anti-inflammatory substances like *UniZyme™* and *Boswellia Serrata Extract* may also help in this regard.

A TENS unit (transcutaneous electro nerve stimulation) can provide significant pain relief, if you haven't tried this yet. You can find TENS units for sale very inexpensively in many pawn shops.

A device that may provide both short-term relief as well as long-term benefit is an inversion device, where you hang upside down, supported by your thighs, or while lying on an "invertible" mat. This will help to pull the vertebrae apart, relieving pressure on the nerve roots for immediate relief.

Also, since the intervertebral disks don't have a very good blood supply, it may help nutrients to reach them—sort of like taking the pressure off a sponge.

Also, look into a treatment modality known as "Prolotherapy." You may find a physician near you who performs this procedure by looking up the *American Association of Orthopaedic Medicine (AAOM)* on the Internet at www.aaomed.org. Members of this group are experts in this procedure.

Ward Dean, M.D.

CarnoSee™ for Glaucoma?

Dear Dr. Dean,

Are the CarnoSee™ eyedrops sufficient for glaucoma, or should they be used along with the capsules? — Ms. G.

Dear Ms. G.,

Glaucoma is a serious condition, and no nutritional program that I am aware of has completely alleviated it. Please continue on whatever treatment regimen your ophthalmologist recommends.

Nevertheless, *CarnoSee™* eyedrops may help with glaucoma. They have been reported to reduce intraocular pressure, one of the signs that usually accompany glaucoma. I also recommend *Forskolin Extract* capsules as Forskolin has also been documented to reduce intraocular pressure. Please see the article on *Forskolin Extract* on VRP's website (www.vrp.com/library/734272.html).

Ward Dean, M.D.

Anabolic Steroids: Anadrol 50

Dear Dr. Dean:

I am a 48-year-old male. I take Anadrol 50 mg once in the morning, plus one sometimes before a workout.

Does Indole-3-Carbinol (I3C) reduce estrogen production that may be a result of taking the Anadrol, and will this reduce DHT, to aid in addressing hair loss?

What are the other positive and negative effects on men of using this product? What dose should be adequate? — Mr. H.

Dear Mr. H.,

Anadrol-50 is one of the most potent anabolic/androgenic steroids known. It can also be pretty rough on the liver.

I3C will not reduce estrogen production—but it will help your body to metabolize the estrogen that is likely to be formed. I3C will not reduce DHT, although VRP's *ProstaCol®* has potent DHT-reducing effects.

As mentioned, Anadrol-50 can also induce liver damage, so I suggest a combination of *HepatoGen™*, plus *N-Acetyl Cysteine*, and possibly additional *Glutathione Plus*, to offset these effects. I'd also suggest monitoring your liver enzymes every three to six months.

Ward Dean, M.D.

For more customer questions and answers, or to ask your own question, visit Vitamin Research Products' website at www.vrp.com and go to "Dear Doctor."

Influenza Vaccine in the News: What To Do About The Flu

by Ward Dean, M.D.

With the much ballyhooed shortage of flu vaccine, many people have asked me for suggestions about what to do to avoid the flu, and what to do about it if they catch it.

First, I don't think the shortage of flu vaccine is such a crisis, because I don't recommend the flu vaccine anyway. A vaccine I *do* recommend, for children and immuno-compromised elderly who believe they are at risk for the flu or other bronchopulmonary infections is the pneumococcal vaccine, *Pneumovax*. *Pneumovax* is well-tested for safety and efficacy against pneumonia—but also appears to have a signifi-

cant cross-reactivity against other viral and bacterial infections. I think it may be more effective than the flu vaccine. It is one of the few immunizations I recommend. It is believed to be good for about ten years.

I think there are a number of other things we can do to reduce the likelihood of contracting the flu. Air ionizers in the home or office may help to neutralize airborne viruses, and reduce transmission of the flu. Also, the use of a cool mist humidifier, filled with a 2-to-1 combination of water and hydrogen peroxide (two bottles of water and one bottle of H₂O₂) is often very helpful.

Also, a combination of protective nutrients like Vitamins A and C, immune enhancers like *Beta Glucan* and *Thymic Protein A*, and anti-viral substances like *Silver Liquid 400 ppm*, *Oregano Oil*, and *Olive Leaf Extract* help to alleviate symptoms and shorten the duration of the flu. I also would suggest *Cat's Claw* extract, or its more potent form, *Samento®*.

For a more complete list of my recommendations, please see my article, *How I Treat Colds and Flu*, at www.vrp.com/library/733207.html.

For more information on *Samento*, see James South's article online at www.vrp.com/library/854642.html.

Modified Citrus Pectin (MCP): Expanding Roles in Cancer and Heavy Metal Toxicity

by Isaac Eliaz, M.D., M.S., L.A.c.

Modified Citrus Pectin (MCP) is derived from the peel and pulp of citrus fruit. MCP is made by processing citrus pectin in a laboratory by either heat and altering pH, or preferably enzymatic degradation (allows for better control of molecular weight and structure) to yield a lower molecular weight pectin.

The MCP used in clinical studies thus far has been exclusively the latter. MCP is used as a dietary supplement because it can be absorbed more readily into the blood stream than citrus pectin.

Unaltered citrus pectin has been used for decades for various uses including as a gelling agent for canning foods, as an anti-diarrheal medicine, and in the production of food and cosmetics. MCP is thought to have many of the similar clinical benefits as regular citrus pectin, as well as additional benefits as a result of its better absorption into the blood stream.

MCP is best known for its effects on inhibiting cancer metastases, reducing tumor growth and development, and possibly immune stimulation. Recently MCP has also shown promise as a chelator of

mercury and other heavy metals. Although more research is needed to ascertain the clinical benefit and usage of MCP for this application, the results thus far have been encouraging.

MCP and Cancer

Clinical studies have shown that MCP may mediate tumor growth, inhibit angiogenesis and block metastasis of cancers. It has been tested on several types of cancers, including melanomas, colon, prostate and breast cancers.

MCP works through a carbohydrate-mediated recognition process by interfering with both cell-to-cell and cell-to-cellular matrix interactions. Specifically, MCP is rich in galactoside residues that have a natural affinity to cancer cells that have galectin-3 receptors. As MCP binds to the cancer cells, it ties up these receptors so that it interferes with the cancer cells' ability to grow and metastasize.¹

In a pilot clinical trial of MCP (PectaSol®) in prostate cancer, patients who had relapsed or had failed prostate cancer treatment were given 15 grams daily (in three divided doses).² The doubling time of PSA (prostate specific anti-

gen) was measured. PSA doubling time (PSADT) is a test that is routinely used to evaluate the growth rate of prostate cancer. In four out of seven patients, the PSADT increased by more than 30 percent, indicating a slowing of the rate of PSA increase (interpreted as a slowing of the progression of the tumor growth). MCP seemed to be most effective in those with the lowest PSA levels. Significantly, three years after completion of the study, all the study participants were still alive for follow-up.²

In a subsequent phase II clinical trial, MCP in a dose of 15 grams per day was tested on 10 men with recurrent prostate cancer. The men had all failed treatment by either radical prostatectomy, radiation or cryosurgery. MCP (PectaSol) was administered, and changes to the PSADT were monitored.

MCP was found to increase the PSADT in eight out of the 10 patients. In half of the patients, the increases ranged from 129 to 941 percent after 12 months of treatment. The authors concluded that MCP may lengthen the PSADT in men with recurrent prostate cancer.³

How MCPs Inhibit Cancer and Metastases

Galectins are present on a number of different types of cancer cells, including prostate, breast, colon, lymphoma, melanoma, glioblastoma and laryngeal epidermoid cancer cells.

When cancer cells metastasize, the number of galectins on their surface increases as the cells grow from early to advanced stages of growth. The galectins have an affinity for binding to carbohydrates, and they are known to be involved in mediating the growth and metastasis of cancer.

The higher number of galectins on cancer cells that are growing reflects their increased ability to move to other sites and bind to them. MCP has an affinity to bind to these cancer cells, and thus block them from moving to new sites and metastasizing. Beyond its effect on metastasis, MCP also has substantial anti-

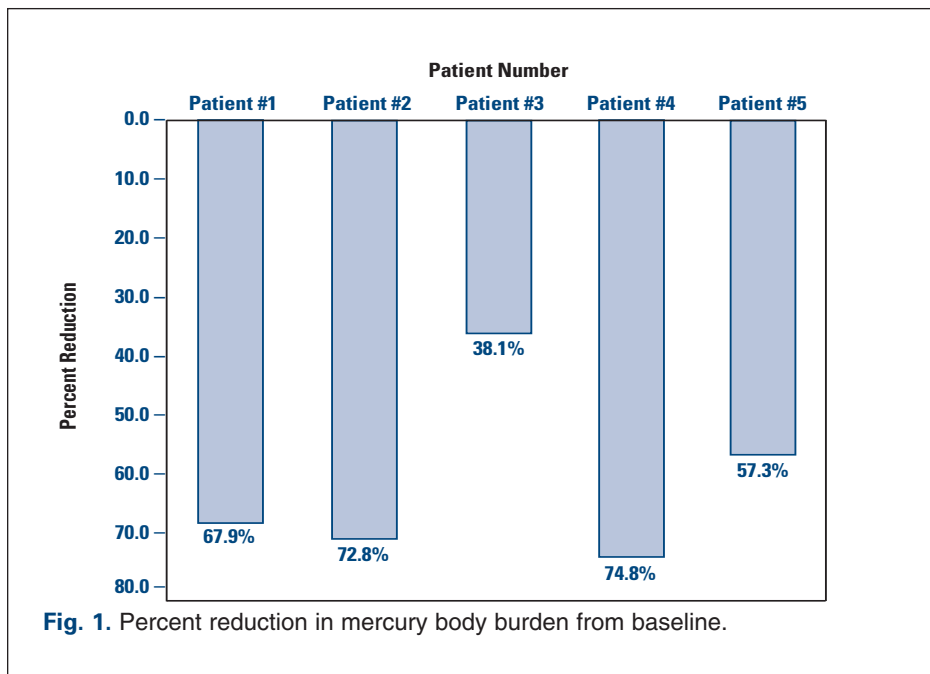


Fig. 1. Percent reduction in mercury body burden from baseline.

angiogenesis effects. Angiogenesis is the process of forming new blood vessels. Tumors are continually growing new blood vessels to bring the fuel they need to grow. MCP will thus affect the primary tumor, and is known to reduce the size of primary tumors. Therefore, MCP may help to control both the growth of the pri-

What began as a commonly used ingredient in foods—citrus pectin—has now become a dietary supplement with clinically proven benefits in a number of areas, including cancer and heavy metal detoxification.

mary cancer as well as inhibit the metastatic process, and can be used at any stage of cancer growth and progression.

One in-vitro study demonstrated MCP's cytotoxic effect on cancer cells, and the effect on adherence and metastasis of the cancer cells. The study used PC-3 cells plated onto a human endothelial cell monolayer with or without 0.1 percent or 1.0 percent MCP. The cytotoxicity of MCP was found to be 80.7 percent at the 1.0 percent concentration, and 76.9 percent at the 0.1 percent concentration. This was compared to 3.8 percent in the control group. The results indicated that MCP has a highly cytotoxic effect on PC-3 cells co-cultured with human endothelial cells.⁴

A New Application for MCP: Heavy Metal Detoxification

The standard western medical procedure for removing mercury from the body to treat mercury toxicity is chelation, performed with chelators like DMSA or EDTA. While this may be the routine and most beneficial procedure when facing a serious acute toxicity problem, MCP also has shown benefit in reducing the body burden of toxic heavy metals.

In a recent clinical study, baseline levels of total body mercury burden were taken and then compared with levels after treatment with MCP (15 grams of

PectaSol daily) for four to 10 months. The total body mercury burden was determined by using a DMPS (2,3-Dimercapto-1-propanesulfonic acid) challenge of 250 mg i.v., followed by six hours of urine collection. The results showed a significant average decrease of over 60 percent (p=0.03) in the total body mercury burden after treatment with MCP (Fig. 1).⁵

In an earlier study, MCP (PectaSol®) was given to patients and proven to increase urinary excretion of heavy metals such as lead, mercury, cadmium and arsenic.

The results of the study found that MCP allowed for safe chelation with no side effects. It was suggested to be a promising alternative to intravenous chelating therapies currently offered as primary therapy for heavy metal toxicity.⁶

The Problem with Mercury

Heavy metals constitute a dangerous insult to the body through DNA damage, hormonal modulation, immune suppression, oxidative stress and hyperinflammation. They are of particular concern in prostate cancer and breast cancer, lymphomas and others. Therefore, MCP has this additional benefit for treating various cancers.

Recent news on mercury is particularly concerning for the US population. In March 2004 the Environmental Protection Agency put out a press release that said nearly all fish contain traces of mercury, and that some contain higher levels—enough to harm an unborn baby or young child's developing nervous system. Because of this they issued a warning for women who may get pregnant, pregnant women and nursing mothers to eat only two meals of fish that are thought to have lower levels of mercury per week.⁷

In the most recent update, on August 24, 2004, the EPA issued a warning that one-third of the nation's lakes and one-fourth of its riverways are contaminated with toxic levels of mercury and other contaminants, and warned pregnant women and children against consuming fish from these sources.

Additionally, a National Academy of Sciences panel definitively warned that some children who had been exposed to mercury while in the wombs of their mothers were at risk of becoming those children "who have to struggle to keep up

in school and who might require remedial classes or special education."

The risk of mercury toxicity from fish has reached epidemic levels. These concerns have been spurred on by two studies. One landmark study conducted by the Centers for Disease Control found that 10 percent of women of childbearing age had levels of mercury higher than the EPA's recommended reference dose (5.8 microg/L).⁸ Another study, published in *JAMA (Journal of the American Medical Association)*, regarding the levels of mercury in U.S. children and women of childbearing age, found that 8 percent of women had potentially dangerous levels of mercury.⁹ Furthermore, women who ate more fish were found to have the higher levels of mercury. Another source of mercury toxicity may be amalgam dental fillings.

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<i>Customers' Corner, pages 8-9</i>	
Product	Code
AGEBlock™	1985
Benfotiamine/Pyridoxamine	
AGE Inhibitor	2118
Beta 1, 3-D Glucan	5043
Beta-Sitosterol	5691
Boswellia Serrata Extract	5041
Calcium/Magnesium	7451
CarnoSee™	9126
Cat's Claw	5061
Chondroitin Sulfate	5701
CoQ10 (Coenzyme Q10)	6303
Essential Minerals	1871
Extend ONE	3200
Forskolin Extract	5881
Glucosamine Complex	3601
Glutathione Plus	4341
HepatoGen™	1600
Indole-3-Carbinol (I3C)	6041
Inositol Hexanicotinate (B3)	1045
N-Acetyl Cysteine	4155
Niacin	1044
Nutri-Joint	5241
Olive Leaf Extract	8241
Optimum 6	3310
Oregano Oil Caps	6461
ProstaCol®	1620
Red Clover Extract	8651
Red Yeast Rice Extract	6271
Samento® Extract	9506
Saw Palmetto	6440
Silver Liquid	1645
Stinging Nettle Extract	5421
Strontium	8731
Thymic Protein A	9122
UniZyme™	1630

MCP

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How MCP Works as a Gentle Chelator

Pectins are natural gelling agents, binders, thickeners and stabilizers in foods. They mostly consist of galacturonic acid and galacturonic-acid methyl esters with average molecular weights from 50,000 to 150,000. High-methoxy (HM) pectin has at least 50 percent DE (degree of esterification) or greater, while a low-methoxy (LM) pectin's DE is 50 percent or less. For dietary supplement purposes, the low-methoxy pectin is used.

These long molecules have a special ability to not only bind water in foods, but other chemicals as well.

In the 1980s after the Chernobyl disaster, pectates were given to children with elevated radioactive readings. Their radioactive levels were decreased by 50 to 60 percent. This led to the idea of using MCP, which gets absorbed systemically, as a systemic chelator. A patented form of MCP mentioned in the above studies confirms this theory.

My observation from using it as a detoxification agent in my clinic is that it works as a gentle chelator in the blood stream, and it is useful for ongoing use. A possible mechanism of action may be that MCP exerts its heavy metal detoxification through gradient changes between the tissue and the blood stream. In the long-term study using MCP for mercury detoxification, there was no limit to the intake of fish and seafood by the patients, and the levels still went down. This has also been my experience in practice.

MCP shows promise in other areas of health, as well, beyond cancer and heavy metal toxicity. Citrus pectin is known to be able to reduce cholesterol levels and enhance the immune system's response. MCP is thought to have similar but even greater benefits, due to its enhanced absorption in the blood stream.

Suggested Use of MCP

What began as a commonly used ingredient in foods—citrus pectin—has now become a dietary supplement with clinically proven benefits in a number of areas, including cancer and heavy metal detoxification. A summary of the expand-

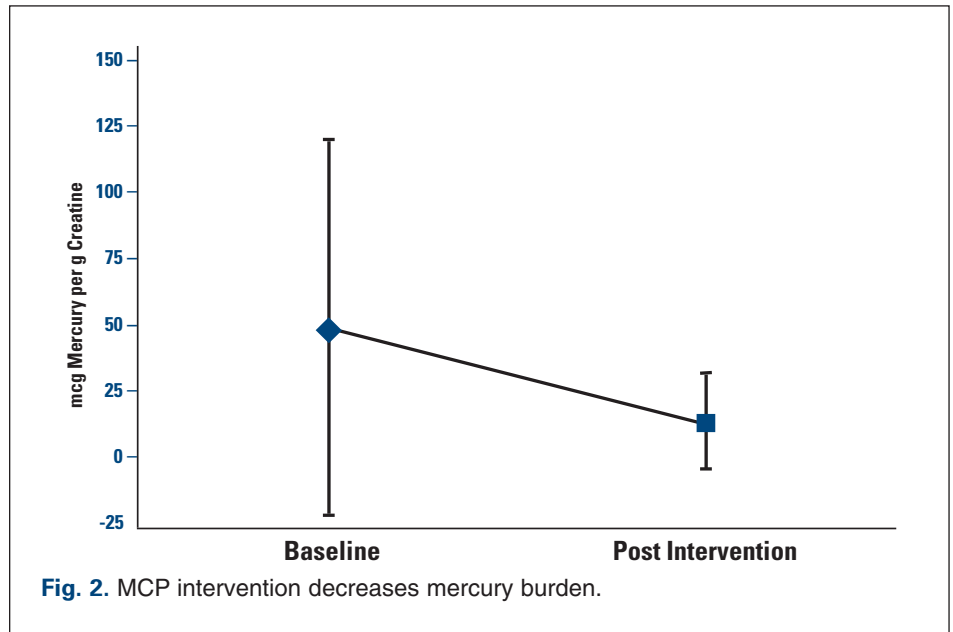


Fig. 2. MCP intervention decreases mercury burden.

ing list of clinical indications for MCP includes:

- Reduce the size or growth of primary tumors
- Prevent or slow metastasis
- Prevent or slow angiogenesis
- Reduce heavy metal load
- Reduce cholesterol
- Enhance immunity.

Although fish are still recommended as part of a healthy diet, and an essential source of certain nutrients, such as essential fatty acids like DHA, mercury levels are becoming a widespread health concern. As the environmental cleanup of mercury is unlikely in the short-term, the medical community should also develop more methods to treat toxicity or reduce high levels of mercury body burden (Fig. 2). One approach is the use of traditional and alternative medicine cleansing programs along with the use of dietary supplements—which may act as gentle chelators—such as EDTA, DMSA and MCP.

For chelation purposes, MCP should be taken in doses of 5 to 15 grams per day, depending on mercury levels, for one year. Maintenance at 2 to 5 grams per day should be enough. I recommend either 15 grams per day, or 15 grams per day for the first three to five days of the month, then 5 grams per day for the remainder of the month.

For use in cancer patients, MCP should be used at the level of 3-5 grams per day for prevention (lower density of Galectin-3 molecules), or 15 grams per day for active disease.

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Isaac Eliaz, M.D., M.S., L.Ac.

Dr. Isaac Eliaz is the medical director of the Amitabha Medical Clinic and Healing Center in Sebastopol, California (www.dreliaz.com). For the last 15 years Dr. Eliaz's medical practice has centered on the integrative treatment of cancer. He has been involved in numerous research studies investigating the effect of various nutritional supplements on cancer and has been granted two patents on his discoveries.

AGEs, Cross-linkages

Continued from page 7

was synthesized in Japan in the 1960s.^{25,26} BFT has been shown in many human and animal studies to have superior bioavailability to thiamine (B1)—the rate of absorption of therapeutic doses (50 to 100 mg) of B1 is relatively small (usually just four to six percent).²⁷

In the body, both B1 and BFT are transformed into thiamine diphosphate (TDP), the coenzyme form of B1. TDP is essential for the activation of an enzyme called “transketolase.” Transketolase protects cells from AGE formation by diverting the products of glucose metabolism—triose phosphates—into the pentose pathway. If not successfully diverted into this pathway, the triose phosphates become AGEs.²⁸

Comparative studies with B1 and BFT indicate the superiority of BFT absorption. One study found a 120-fold increase in TDP levels in red blood cells from BFT compared to B1,²⁷ and another study with end-stage renal disease patients found that BFT had 430 percent better overall absorption than B1.²⁶ Other scientists reported that “all biokinetic data demonstrated a significantly improved thiamine bioavailability from benfotiamine compared with other preparations.”²⁹

BFT is not only superior to regular B1 in improving TDP-coenzyme B1 status, but it has also been shown to be highly effective in the prevention of AGEs and functional damage in experimental animals³⁰ and humans.³¹⁻³³

In one study of Type 1 diabetics, doses of BFT of 600 mg per day for 28 days resulted in a 40 percent reduction of red blood cell levels of the AGE, carboxymethyllysine (CML), and 69 percent reduction of intracellular levels of methylglyoxal-derived AGEs.

Significantly, CML levels inversely correlate with diabetic blood vessel damage, and methylglyoxal-AGE is the most important intracellular AGE.³¹ Other studies of diabetics with peripheral neuropathy showed reduction of pain, increased vibratory sensitivity and normalization of cardiac rhythm.^{32,33}

A safe and effective human dose of BFT is believed to be approximately 100 mg, taken two or three times daily.

Carnosine

The anti-aging effects of carnosine were detailed in the article in the October 2004 *Vitamin Research News* (online at www.vrp.com/library/1060676.html). Dr. Alan Hipkiss of the Division of Biomolecular Sciences, King's College, London, reviewed the anti-aging effects of carnosine and aminoguanidine. He agrees that one of the major mechanisms of carnosine's anti-aging properties is its powerful effects as a cross-link inhibitor and breaker. He suggested that the combined use of carnosine and aminoguanidine might help to control age-related molecular dysfunction.

Cinnamon Extract (Cinnulin PF®)

Cinnamon has been known to restore insulin sensitivity, normalize blood glucose and insulin levels, and normalize lipid profiles in animals and humans.³⁴⁻³⁸ Cinnamon Extract (Cinnulin PF®) is a patented cinnamon extract that has even more potent effects than raw cinnamon.³⁹ A 250 mg daily dose of Cinnulin PF divided between two or three meals has been found to help regulate blood insulin, glucose and lipids, and should further help to reduce the formation of AGEs.

Conclusion

The venerable cross-linkage theory of aging has clearly gained new respectability in light of the advances in understanding of non-enzymatic glycation and the formation of AGEs and AGE-induced cross-links. Research in this area is leading to the development of new classes of cross-linkage inhibitors and breakers as anti-aging drugs and nutrients.

It is also interesting to note the close relationship between the cross-linkage, neuroendocrine and free radical theories. Free radicals have been proposed as a cause of cross-linkages, as well as a factor in the loss of sensitivity of receptors of various hormones and neurotransmitters.

Also, the loss of insulin receptor sensitivity and impaired glucose metabolism proposed by the neuroendocrine theory, which results in high levels of blood sugar, is clearly a cause/accelerator of cross-linkages.

Understanding these processes clearly points at a number of ways to attempt to delay, and in some cases, perhaps even reverse aging. One of the most effective

approaches, we believe, is to maintain low levels of glucose and insulin, and minimize the formation of cross-linkage-inducing advanced glycation end products (AGEs).

In addition to a low-glycemic diet and exercise, we believe a potent anti-aging combination will be found using either Metformin, aminoguanidine, or standardized Goat's rue extract, along with P5P, pyridoxamine, carnosine, cinnamon extract, plus additional thiamine or benfotiamine. In the future, cross-linkage breakers like ALT-711 may also become clinically available.

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Green Tea Update: Studies Continue To Show Ancient Tea's Link to Health

by Kimberly Pryor

Cultures around the world have long appreciated tea. It is thought that tea drinking originated in ancient China and from there it spread throughout the world. A Buddhist priest returning from China brought the first tea seeds to Japan after observing its use during religious meditation.

There are many varieties of tea, including red and black tea, but no tea has been more researched than the green variety.

Studies have shown that green tea is rich in polyphenolic compounds, and its main constituent is epigallocatechin-3-gallate (EGCG), which has powerful antioxidant properties. In past studies, EGCG and green tea polyphenols have exhibited anti-inflammatory effects, played a role in colon health, and helped with weight-loss efforts.

In the past several months alone, many new studies have been published in the medical literature reporting on this ancient drink. In current studies, researchers have explored green tea's ability to assist with healthy blood sugar levels, protect neurons in experimental animals, support the health of the prostate and ovaries and to influence the damaging effects of LDL cholesterol.

Blood Sugar

In a study published in August 2004, a 1.5-gram dose of green tea promoted healthy glucose metabolism during oral

glucose tolerance tests in healthy human volunteers.¹ In the same study, green tea also lowered blood glucose levels in diabetic mice two to six hours after administration at 300 mg/kg without affecting

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serum insulin levels. No effect was observed in control mice. Based on other results of the study, the scientists suggested that green tea's ability to influence levels of a blood serum protein may be involved in its blood-sugar-supporting role.

Brain Health

Studies have indicated that oxidative stress resulting in inflammation may play a pivotal role in neurodegenerative diseases.² This has recently led scientists to investigate how antioxidant polyphenols

such as those found in green tea can support brain health. In animals, the green tea polyphenol EGCG protected against neuronal damage and brain edema after unilateral cerebral ischemia (stroke).³ In another study, researchers treated mice with a substance that impairs the animals' cognitive function.⁴ Chronic administration of green tea polyphenols significantly reversed this induced retention deficit. Furthermore, the green tea polyphenols dramatically inhibited the activity of an enzyme (acetylcholinesterase) that leads to the inactivation of acetylcholine, a neurotransmitter important in brain health.

Prostate Health

In the September issue of the *International Journal of Cancer*, researchers investigated how the green tea component EGCG affected cyclooxygenase (COX-2) in human prostate cancer cells.⁵ Overexpression of COX-2 has been implicated in many conditions, including cancer. In the study, researchers demonstrated that EGCG inhibits COX-2 without affecting COX-1 expression in androgen-sensitive and androgen-insensitive human prostate cancer cells.

In another study published in the December 2004 *International Journal of Cancer*, EGCG from green tea affected the activity and expression of Prostate-Specific Antigen (PSA).⁶ PSA is able to

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AGEs, Cross-linkages

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Featured Products

Modified Citrus Pectin

Modified Citrus Pectin is easily absorbed in the gastrointestinal tract and is useful for energy metabolism as well as a laxative.*

Start with two teaspoons per day, mixed with 8 oz. of water, juice or other liquid beverage. Gradually increase to four to six teaspoons, or as recommended by your health-care professional. For daily maintenance, one to two teaspoons can be used. At two teaspoons per day, this is a 40-serving supply.

• 5590 200 grams \$36.95

AGEBlock™

AGEs (Advanced Glycosylation Endproduct) are end products that happen when there are ongoing, high levels of sugars and hormones in the body.* Doctors use the term "end product" when referring to the end, or last step, of a metabolic pathway. Glycosylated end products are known to have long-term, damaging effects.* The ingredients in AGEBlock have been shown to support healthy vascular function and protect the body from these adverse endproducts.*

Recommended dosage: One capsule, three times per day.

• 1985 90 capsules \$29.95

Cinnamon Extract (Cinnulin PF®)

Cinnulin PF® is a water-soluble cinnamon extract, developed with assistance from noted cinnamon researcher Dr. Richard Anderson.

Recommended dosage: Take six capsules per day with meals in divided doses. Persons who eat three meals per day should take two capsules with each meal. Persons who eat two meals per day should take three capsules with each meal. The makers of Cinnulin PF® recommend a total daily intake of 250 mg.

• 5057 180 capsules (42 mg) \$19.95

Cinnulin PF® is a registered trademark of Integrity Nutraceuticals International, U.S. serial #783588235, manufactured under U.S. patent #6,200,569.

AdaptaPhase® I

From behind the Iron Curtain comes one of the most closely-guarded secrets of the Cold War.

The Russian space program and top-secret Russian Olympic athletic research developed powerful anti-aging formulas based on adaptogens. Nobel-caliber research has yielded this unique proprietary blend of adaptogenic herbs, Eleutherococcus senticosus, manchuian thorn tree extract, hawthorn extract, echinopanax elatum and schisandra. This liquid herbal formula is designed to be used every day for maximum stress protection and stress relief.*

Recommended dosage: One or more droppers full several times per day as needed.

• 1910 30 ml liquid (1 fluid ounce) \$21.95
• 1911 120 ml liquid (4 fluid ounces) \$69.95



Samento®

From deep with the rainforest and refined by scientific knowledge, comes Samento®. Samento® is a proprietary extract of uncaria tomentosa, also known as cat's claw, in an easy-to-take full-spectrum liquid extract. It's the pentacyclic (POA) form of cat's claw that has been shown to support critical immune function, and Samento® delivers the pentacyclic constituents, certified free of TOA (tetracyclic oxindole alkaloids).* Shake well before each use.

Recommended dosage: One to three times per day, put up to five drops in four ounces of pure water. Wait one minute and drink. Best if taken on an empty stomach.

• 9506 30 ml (1 fluid ounce) \$44.95

Benfotiamine/Pyridoxamine AGE Inhibitor

Benfotiamine and pyridoxamine inhibit the production of advanced glycation end products (AGEs) and advanced lipoxidation end products (ALEs) within the human body. AGEs/ALEs accumulate over a lifetime, cross-linking and gradually damaging long-lived body proteins, such as collagen and elastin.* **Each capsule contains 100 mg benfotiamine and 100 mg pyridoxamine.**

Recommended dosage: Take one capsule two or three times per day.

• 2118 60 capsules \$29.95

Lipoic Acid

Lipoic acid is a highly effective, biologically available and well-researched antioxidant that works in both the fat and water soluble portions of human cells. Lipoic acid supports healthy liver regeneration, immune function and circulation, as well as vision and glucose metabolism.* It also supports cardiovascular and neurological health.* Being a powerful antioxidant, it protects and repairs cells and reduces damage caused by oxidation.* Lipoic acid also improves the effectiveness of vitamin C and E, two well-known antioxidants.

Recommended dosage: One to six capsules per day.

• 3451 60 caps (100 mg) \$11.95
• 3455 90 caps (500 mg) \$59.95

Green Tea Extract

Research indicates that green tea is a more potent antioxidant than vitamin E.* VRP's Green Tea Extract contains an industry-leading potency of 98 percent polyphenols, 90 percent catechins and 55 percent EGCG with only 1 mg caffeine per capsule.

Recommended dosage:

One to three capsules per day with meals.

• 6351 120 capsules (180 mg) \$13.95

*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.

Green Tea

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affect cell migration, metastasis, and other processes important in cancer. In addition to restraint of PSA expression, EGCG was found to inhibit in a dose-dependent manner these PSA processes that occur during cancer, at concentrations close to levels measured in the serum following green tea ingestion.

Ovarian Health

In a study published in the November issue of the *International Journal of Cancer*, scientists studied 254 patients in China who had confirmed epithelial ovarian cancer.⁷ The subjects were followed for a minimum of three years. The variables examined included the subjects' survival time and the frequency and quantity of tea consumed post-diagnosis. The researchers determined which participants had died and adjusted for factors such as age at diagnosis and body mass index.

The rate of survival differed between green tea drinkers and non-drinkers. Among green tea drinkers, 81 of 104 (77.9 percent) survived to the time of interview. On the other hand, only 67 subjects (47.9 percent) were still alive among the 140 non-tea drinkers.

There also appeared to be a relationship between the dose of green tea consumed and the survival rate.

LDL Cholesterol

A recent study published in a Chinese medical journal provides further support that green tea also has a positive effect on the way the body handles LDL "bad" cholesterol.⁸

Researchers decided to investigate whether green tea polyphenols could influence the proliferation and migration of vascular smooth muscle cells (VSMC). One of the major mechanisms of arterial thickening in atherosclerosis is this proliferation and migration of these cells. Elevated plasma levels of low-density lipoprotein (LDL) (the "bad" cholesterol) stimulate the proliferation of vascular smooth muscle cells. Consequently, researchers treated vascular smooth muscle cells from rats with LDL in the absence or presence of green tea polyphenols. The researchers then determined the cell proliferation rate. Compared with the cells not treated with green tea, the proliferation of the VSMCs induced by LDL was dose-dependently inhibited by green tea polyphenols.

The researchers concluded, "Green tea polyphenols may, therefore, offer vascular protection by inhibiting VSMC growth in response to hypercholesterolemia."

Green Tea Extract

Vitamin Research Products is introducing a new, more potent green tea extract standardized for all three main green tea components: polyphenols (98 percent), catechins (90 percent) and EGCG (55 percent). EGCG and catechins are the most widely researched green tea components, and this new standardization provides a hefty dose of these important green tea constituents.

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