

LE Magazine February 2003

REPORT

A 20th Anniversary



It's hard to believe that 20 years has gone by since the first version of Life Extension Mix™ was introduced.

Way back in 1983, Foundation members were clamoring for a comprehensive, high-potency supplement that would provide the most important disease-fighting nutrients. At that time in history, millions of Americans were learning about the value of dietary supplements through a best-selling book called *Life Extension* (Durk Pearson and Sandy Shaw).

In response to the scientific data presented in this book, Life Extension Foundation members were taking dozens of different pills each day to obtain the potencies shown in research studies to be effective. With the introduction of Life Extension Mix, members were able to reduce the number of pills swallowed each day, obtain a wider variety of nutrients and save money.

Since its introduction 20 years ago, the Life Extension Mix formula has been updated 15 times to reflect new findings about preventing the degenerative diseases of aging.

Back in 1983, there were fewer than 3000 Life Extension members. Today, over 78,000 people are enrolled, representing a collective group of over 200,000 individuals (when family members are included).

We are proud of the fact that so many members are still with us, and in good health. For the benefit of newer members who are not familiar with Life Extension Mix, a summary of the scientific data relating to the nutrients contained in this formula begins on the following page.

People join the Life Extension Foundation to discover scientific methods of preventing and treating age-related disease. One of the most cherished benefits of Foundation membership is the opportunity to obtain high potency supplements at low prices. Many commercial dietary supplements do not provide enough of the active ingredient for the consumer to obtain the expected health benefit. For instance, the Life Extension Foundation introduced a plant extract called lutein in 1985 to help protect against macular degeneration. The amount of lutein contained in a daily dose of Life Extension Mix™ is over 15,000 micrograms, which is double the minimum amount scientists say is needed to protect against this debilitating eye disease. The most popular lutein-containing commercial supplement, on the other hand, contains only 250 micrograms per daily dose. Life Extension Mix thus provides 61 times more lutein than the most popular brand.

The importance of purity

A growing concern among physicians and consumers is whether dietary supplements contain all of the active ingredients listed on the label. This apprehension is based on well-publicized analyses of commercial supplements showing considerable variation in ingredient quality and quantity.

The Life Extension Foundation learned a long time ago that there were few ingredient suppliers who can be trusted to consistently deliver quality ingredients. That is why extraordinary quality-control measures were implemented in order to guard against the counterfeiting that has become so prevalent in the supplement industry.

Companies offering low-cost ingredients constantly solicit Life Extension's business. An assay of the ingredients from these discount companies, however, using HPLC (high performance liquid chromatography) or mass spectrophotometry (mass spec), often reveals inconsistencies. This is why Life Extension restricts its purchases of ingredients to nutrient suppliers that take extra steps in their manufacturing process to ensure the active ingredients are of high quality and potency.

When members buy products from the Life Extension Buyers Club, they have assurance that the quality of the product is backed by the organization's commitment to achieving an indefinitely extended life span. Members receive large discounts that enable them to purchase premium nutrient supplements at prices below those charged by commercial companies.

The most popular life extension supplement

Health-conscious people often spend a lot of time and money taking many individual bottles of pills. To make it convenient and economical to obtain the nutrients you need, the Life Extension Mix formula was developed to provide optimal potencies of the most important dietary supplements.

Life Extension Mix provides important nutrients like vitamin C, vitamin E, complete B-complex and carotenoids, along with important minerals, amino acids and herbs. What clearly separates Life Extension Mix from commercial products are disease-fighting plant extracts that cannot be found in any other multi-nutrient formula.

Despite the fact that Life Extension Mix contains high potencies of nutrients along with exclusive plant extracts, members pay far less money for this formula than if they bought these nutrients separately.

What's missing from commercial supplements?

Consuming lots of fruits and vegetables dramatically lowers the risk of degenerative disease. This fact has been documented in epidemiological studies showing that people are healthier if they incorporate more of the right kinds of plants into their diets.

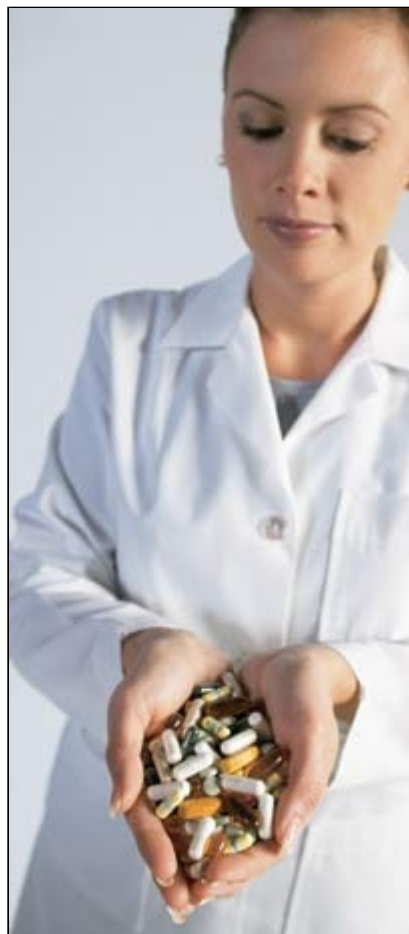
The problem is that few people consistently eat enough fruits and vegetables to protect against age-related diseases such as stroke, cancer, macular degeneration and heart attack.¹ This is one reason why vitamin supplements are becoming so popular in the United States. The concern about multi-vitamin formulas, however, is that they do not provide all the vital plant components needed to maintain good health.

Scientists have identified many fruit and vegetable extracts that protect cells against the deleterious effects of aging. Life Extension Mix is the only multi-nutrient formula that provides these new disease-preventing agents from plants.

Moving beyond vitamins

Researchers have moved beyond traditional nutrients in their quest to discover additional ways of protecting against disease. One botanical extract that offers tremendous potential is D-glucarate. This extract appears to protect against cancer and other diseases via different mechanisms than antioxidants.

D-glucarate is found in grapefruit, apples, broccoli and brussels sprouts.^{2,3} Consumption of these types of fruits and vegetables confers a protective effect against cancer, and D-glucarate is a component of these foods that has scientists very excited.





The body is bombarded with carcinogens on a daily basis. These cancer-causing agents include pesticides, overcooked food, alcohol, food additives, tobacco, fungal mutagens and industrial pollutants. While avoiding carcinogens is difficult, it may be possible to mitigate their lethal effects by providing the body with plant extracts that facilitate the detoxification and removal of these dangerous substances from the body.

D-glucarate protects against cancer-causing agents in a way that is separate from the effects of antioxidants (vitamins C & E and carotenoids) and methylation-enhancing agents (folic acid and vitamin B12). D-glucarate works by supporting the detoxification and removal of dangerous chemicals, and also by protecting against the mutating effects that these carcinogens induce on cellular DNA.³

D-glucarate is being used in a Phase I human trial at Memorial Sloan-Kettering Cancer Center in women at high risk for developing breast cancer. This study is in collaboration with the National Cancer Institute and National Institutes of Health. Life Extension Mix provides 200 mg of standardized D-glucarate per daily dose, in addition to the naturally occurring D-glucarate found in the new vegetable concentrates that are included in the formula.

The DNA protecting effects of ellagic acid

Ellagic acid is a cancer-preventing compound found in red raspberries, strawberries and other fruits.^{4,5} Ellagic acid acts as a detoxifying agent by binding to carcinogens and making them inactive.^{6,9} Molecular studies show that ellagic acid prevents binding of carcinogens to DNA,^{10,11} reduces the incidence of cancer in cultured human cells exposed to carcinogens, and has antimutagenic properties.¹²⁻¹⁶ Epidemiological studies show that people who consume fruits high in ellagic acid have lower rates of cancer and heart disease.

Clinical tests conducted at the Medical University of South Carolina (MUSC) show that ellagic acid may help prevent cancer, inhibit the growth of cancer cells and arrest the growth of cancer in persons with a genetic predisposition to the disease. These studies show that ellagic acid induces cervical cancer cells to undergo apoptosis (normal cell death).¹⁷ Tests reveal similar results for breast, pancreas, esophageal, skin, colon and prostate cancer cells.¹⁸⁻²⁶ Life Extension Mix contains 50 mg of a raspberry extract that provides 97% ellagic acid.

Continued on Page 2 of 3

[Back to the Magazine Forum](#)

REPORT

A 20th Anniversary

Broccoli: a wealth of phytochemicals



Broccoli may contain more cancer-preventing nutrients than any other plant. In 1992, scientists identified a broccoli compound called sulforaphane that helps mobilize the body's natural cancer-fighting resources and reduce the risk of developing cancer.²⁷⁻³³

Sulforaphane has been shown to block the formation of tumors initiated by chemical carcinogens. Moreover, sulforaphane has been demonstrated to induce cancer cell death via apoptosis (natural cell death).^{33,34} A large amount of data shows that sulforaphane and other broccoli compounds act as cancer chemopreventive agents by favorably modifying carcinogen metabolism via modulation of both Phase I and Phase II detoxification enzyme systems.³⁵⁻³⁹ This suggests that broccoli compounds prevent cancer by activating detoxifying enzyme systems and inducing cancer cell apoptosis.

Inhibiting DNA-adduct formation reduces incidence of mammary tumors. Sulforaphane was shown in one study to inhibit chemical-induced DNA adduct formation by 68% to 80%, suggesting that this broccoli extract may function as a breast cancer preventive

agent.³⁷ On the basis of mechanisms of carcinogenic effects of cigarette smoke, sulforaphane appears to be a component in the prevention of lung cancer.

Broccoli contains the highest percentage of D-glucarate of any plant studied, along with a cornucopia of carotenes and other nutrients that provide a wide range of health benefits. Life Extension Mix contains a concentrated broccoli extract that is standardized to deliver precise amounts of sulforaphane and D-glucarate in each dose.

Cancer-fighting flavonoids

Apigenin is a flavonoid found in parsley, artichoke, basil, celery and other plants. A large number of published studies have demonstrated the anticancer properties of apigenin. Luteolin is a flavonoid found in many of the same foods that contain apigenin. While luteolin produces effects similar to apigenin, it has its own unique beneficial properties as well.

When apigenin was tested against other flavonoids on the growth of human breast cancer cells, apigenin showed the most effective antiproliferative effects.⁴⁰ Other studies show that apigenin or luteolin bind to estrogen receptor sites on cell membranes in order to prevent overproliferation of these cells.⁴¹

Apigenin and luteolin have been tested against a wide range of different types of cancer, and these flavonoids have consistently been shown to induce cancer cells to differentiate into normal cells and undergo apoptosis (programmed cell death). When measured against 27 citrus flavonoids, luteolin had the most potent antiproliferative activities against several tumor cell lines.⁴²

Luteolin may help prevent breast cancer. Several studies show that luteolin reduces excess estrogen formation and blocks the binding of estrogens to breast cell receptor sites.^{43,44} Life Extension Mix has the most concentrated bioflavonoid complex ever put into a dietary supplement and includes standardized extracts of luteolin and apigenin.

Enhancing glucose metabolism

Glucose that is not absorbed by cells is eventually converted into body fat. Aging cells lose their ability to utilize insulin for the purpose of absorbing glucose.^{45,46} This insulin-resistance is a direct cause of Type II diabetes, obesity, atherosclerosis and a host of age-related diseases.

Some of the underlying mechanisms required by cell membranes for youthful glucose metabolism have been identified, and Life Extension Mix contains well-documented nutrients to help break down age-related insulin resistance.

Biotin is a B-complex vitamin that provides health benefits ranging from the control of blood sugar levels to the improved appearance of hair and nails.⁴⁷⁻⁵¹ In order to improve glucose utilization in aging people, Life Extension Mix contains 3000 mcg of biotin in each daily dose.

Chromium has been shown to improve peripheral insulin sensitivity, a parameter that is unlikely to be directly influenced by biotin. Thus, the joint administration of high doses of biotin and chromium is likely to combat insulin resistance, enhance glucose uptake by both liver and skeletal muscle and inhibit excessive hepatic glucose production.⁵² There are 200 elemental micrograms of chromium in the daily dose of Life Extension Mix.

Protecting against mitochondrial aging

Massive free radical damage occurs in the cells' energy power plants (the mitochondria), which can overwhelm the cells' antioxidant defense systems. Mitochondrial damage due to aging is a serious health problem in elderly people, whose energy levels decline precipitously even when they remain disease-free.⁵³ The amino acid N-acetyl-cysteine has been shown to stimulate glutathione production for the purpose of providing protection against free radicals that are continuously being generated in mitochondria.^{54,55}

Free radical damage is both a causative and contributing factor in the development of degenerative disease. Scientists are now concentrating on specific free radicals, the different part of the cell that these free radicals attack and the types of antioxidants that are needed to provide intra- and inter-cellular protection against oxidative stress. Life Extension Mix provides antioxidants, such as 600 mg of N-acetyl-cysteine and 500 mg of taurine per daily dose, to protect against differing types of free radicals both inside and outside of cells.⁵⁶

Facilitating youthful methylation

Enzymatic and genetic activity throughout the body depends on the continuous re-methylation of DNA. The age-related breakdown of youthful methylation metabolism predisposes the body to a wide range of degenerative diseases. Maintaining healthy methylation patterns protects against DNA mutations that damage cells and can cause cancer.

Vitamin B12 works synergistically with folic acid and TMG to enhance DNA methylation and reduce toxic homocysteine in the blood. Scientific studies confirm that orally administered vitamin B12 supplements are effectively absorbed by more than 99% of humans.⁵⁷ Vitamin B12 plays a critical role in many enzymatic processes required to maintain good health. Elderly people can suffer from severe neurological impairment if they are deficient in vitamin B12.⁵⁸

Life Extension Mix contains high doses of folic acid and three different types of vitamin B12 along with a small amount of trimethylglycine (TMG).

Keep the blood flowing

As people grow older, their blood platelets become "sticky" and develop the propensity to clot inside blood vessels. While conventional doctors accept this as a normal consequence of aging, the scientific facts are that the risks of stroke and heart attack could be reduced dramatically by adhering to a program that inhibits abnormal platelet aggregation. Life Extension Mix contains a variety of nutrients such as ginger, grape-seed and bilberry that inhibit platelet aggregation.

Dr. Linus Pauling's last great work was to show that specific components in the blood called apolipoproteins are involved in atherosclerosis and aortic valve stenosis. Dr. Pauling showed that vitamin C and lysine can protect against apolipoprotein-induced vascular disease.⁶⁰ Life Extension Mix contains the amount of lysine (500 mg) found in most lysine supplements. Those with valvular stenosis or atherosclerosis may want to take additional lysine.

Magnesium deficiency is a prime culprit in the epidemic of arterial disease that plagues the Western world. Life Extension Foundation members have obtained high doses of magnesium ever since Life Extension Mix was introduced. Different forms of magnesium have shown other beneficial effects at the cellular level in addition to vascular protection.^{61,62} Life Extension Mix contains magnesium arginate, magnesium taurinate and magnesium glycinate to provide magnesium to different parts of the cell.

Modulating immune function

The immune system has been extensively studied over the past 20 years, and scientists have shown how specific nutrients can enhance components of immune function decimated by normal aging.

Zinc and selenium supplements, for instance, when given to elderly populations, significantly reduce the incidence of infectious disease.⁶³ One of the most important disease-preventing nutrients is selenium. While too much selenium can be toxic, it appears that most people take too little supplemental selenium out of concern over toxicity. Life Extension Mix contains 200 elemental



micrograms of three different types of selenium and 35 elemental milligrams of zinc from two different forms of zinc to ensure maximum absorption.

Age-related autoimmunity can create a state of chronic inflammation throughout the body. New studies relate subclinical chronic inflammatory disease to the development of senility, atherosclerosis, aortic valve stenosis, some cancers and a host of other known inflammatory diseases such as arthritis and colitis.⁶⁴⁻⁶⁷ Life Extension Mix contains nutrients that can be taken to safely alleviate chronic inflammatory disease at the cellular level.

Choosing a multi-nutrient formula

There are a number of factors to consider when deciding on a multinutrient formula that you may be taking for the rest of your life. A significant concern among vitamin consumers is the quality of the individual ingredients that are contained in the formula. Life Extension Mix contains only top quality nutrient and herbal extracts.

Another factor to consider is whether the potencies contained in a multinutrient formula are adequate to provide the desired health benefit. The Life Extension Foundation reviews thousands of published studies in order to determine the ideal potencies of each vitamin, mineral, amino acid and plant extract that is blended into the Life Extension Mix formula. Most commercial multi-vitamin preparations do not provide enough lutein, lycopene and other expensive nutrients to produce a statistically significant disease risk reduction effect.

In some cases, minor modifications can mean a big difference in the benefit one obtains from a multi-nutrient formula. For instance, most people readily convert vitamin B6 to an enzymatically active form the body needs called pyridoxal-5-phosphate. Some people, however, do not convert vitamin B6, so Life Extension Mix contains enough biologically available pyridoxal-5-phosphate to ensure that no one taking this formula will suffer from a vitamin B6 deficiency. The same is true with pantothenic acid. While Life Extension Mix provides a huge dose of pantothenic acid, it also provides a small amount of the more biologically active pantothen.

The most important reason one should choose a particular multinutrient formula is the state-of-the-art ingredients it provides. Thousands of published studies show that the risk of contracting cancer, stroke, ocular disorders and heart disease can be reduced by the proper intake of vitamins, minerals, amino acids and plant extracts. The difficulty for most people is that they don't know which nutrients are most important, or how much of each nutrient to take. Commercial supplement companies have fallen behind in keeping up with the breakthroughs in preventive medicine appearing in the medical literature. Life Extension Mix has been updated 15 times since its introduction in 1983 to provide the best disease-prevention nutrients known to science.

Despite the fact that costly top quality nutrients are used in Life Extension Mix, Life Extension Foundation members find that they save a considerable amount of money compared to the cost of other multinutrient formulas. Life Extension Mix provides more potency for less money than commercial formulas, while providing unique health-protecting extracts from plants.

The most recently added ingredients

The most recent ingredient added to Life Extension Mix has scientists so excited, that the National Cancer Institute and U.S. Department of Agriculture are spending millions of dollars to study its potential effects.

As most health conscious consumers are aware, a compelling body of evidence substantiates the ability of selenium to prevent a wide variety of diseases. Unlike most other supplements, selenium comes in a range of biological forms that perform very different functions in the body. The Life Extension Foundation recognized this fact in the early 1980s and included several forms of selenium in multi-nutrient formulas designed to reduce disease risk.

Over the past year, a new form of selenium has been identified that may be a highly effective cancer preventive. In addition, this new form of selenium has demonstrated unique properties that may someday result in it being used as an adjuvant cancer cell killing therapy.

The name of this new selenium compound is Se-methylselenocysteine. We call it SMSC for short. SMSC is the naturally occurring selenium found in plants such as broccoli, garlic and onions. Like chlorophyllin, SMSC has been shown to prevent DNA adduct formation that can lead to the development of cancer.⁶⁸ When compared to other forms of selenium, SMSC prevented mammary cancer in rodents better than any other form of selenium tested.^{69,70} SMSC has been shown to induce apoptosis (programmed cell death) to cancer cells in culture.^{68,71-74}

What makes SMSC different from other forms of selenium is that it is not incorporated into the body's proteins. Critics of selenium supplementation have stated that the body cannot benefit from more than 55 mcg a day of selenium because that amount saturates the body's proteins. SMSC is not incorporated into any protein and is therefore completely bioavailable for chemoprevention and the synthesis of antioxidant enzymes such as glutathione peroxidase.^{75,76}

This new cancer-fighting form of selenium has been added to Life Extension Mix. That means that at no additional cost, Foundation members can obtain this improved form of selenium (SMSC).

An increasing body of research indicates that vitamin D3 has potent and unique cancer preventing properties.⁷⁷⁻⁷⁹ In the past, scientists were overly cautious about supplementation with vitamin D because of potential toxicity. A recent study showed that even massive doses (as much as 10,000 IU a day) might be safe for some people. The potency of vitamin D3 has been increased to 400 IU in the daily dose of Life Extension Mix.

What is Life Extension Mix?

For the enlightenment of new members, Life Extension Mix is a multi-ingredient composition of extracts from vegetables, fruits, herbs and other food concentrates that have been documented in published scientific studies to prevent disease and slow premature aging. In addition, Life Extension Mix provides pharmaceutical potencies of the vitamins, minerals and amino acids that have demonstrated significant health benefits. Most Foundation members use Life Extension Mix as the cornerstone of their overall program to attempt to live longer in optimal health.



Life Extension Mix has been designed, tested and personally used by those who insist on the strictest standards of purity for every nutrient included in the formula. Some people erroneously refer to Life Extension Mix as a multivitamin supplement, but a careful review of its ingredients shows that the formula is light-years ahead of any other nutrient formula on the market. Every ingredient in Life Extension Mix is based on scientific findings about the role that specific nutrients play in defending the body against degenerative disease.

New members are pleasantly surprised when they discover that Life Extension Mix can replace many of the individual supplements they were previously taking. The convenience of obtaining potent doses of nutrients is the prime motivation for taking Life Extension Mix. Another reason that Life Extension Mix is so popular is that it saves the serious supplement user hundreds of dollars a year compared to the cost of buying the ingredients in the formula on an individual basis.

Life Extension Mix makes it practical to follow a scientifically designed disease prevention program. The Life Extension Mix formula has been continuously improved over the past 20 years to provide protection against newly identified mechanisms that have been implicated in the development of degenerative disease.

Continued on Page 3 of 3

[Back to the Magazine Forum](#)

REPORT

A 20th Anniversary

References

1. Li R, et al. Trends in fruit and vegetable consumption among adults in 16 US states: Behavioral Risk Factor Surveillance System, 1990-1996. *Am J Public Health* 2000 May;90(5):777-81.
2. Walaszek Z, et al. D-glucaric acid content of various fruits and vegetables and cholesterol-lowering effects of dietary D-glucarate in the rat. *Nutrition Research (United States)* 1996, 16/4 (673-681).
3. Dwivedi C, et al. Effect of calcium glucarate on beta-glucuronidase activity and glucarate content of certain vegetable and fruits. *Biochemical Medicine and Metabolic Biology (United States)* 1990, 43/2 (83-92).
4. Loarca-Pina G, et al. Inhibitory effects of ellagic acid on the direct-acting mutagenicity of aflatoxin B1 in the Salmonella microsuspension assay. *Mutat Res* 1998 Feb 26;398(1-2):183-7.
5. Maas, J. L, et al. Ellagic acid, an anticarcinogen in fruits, especially in strawberries: a review. *HortScience* vol. 26 (1): p.10-14, 1991.
6. Constantinou A, et al. The dietary anticancer agent ellagic acid is a potent inhibitor of DNA topoisomerases in vitro. *Nutrition and Cancer (United States)* 1995, 23/2 (121-130).
7. Stoner GD, et al. Lung tumors in strain A mice: application for studies in cancer chemoprevention. *J Cell Biochem Suppl* 1993;17F:95-103.
8. Barch DH, et al. Ellagic acid induces NAD(P)H:quinone reductase through activation of the antioxidant responsive element of the rat NAD(P)H:quinone reductase gene. *Carcinogenesis* 1994 Sep;15(9):2065-8.
9. Teel R.W, et al. Ellagic acid metabolism and binding to DNA in organ explant cultures of the rat. *Cancer Letters (Ireland)* 1987, 36/2 (203-211).
10. Barch D.H, et al. Structure-function relationships of the dietary anticarcinogen ellagic acid. *Carcinogenesis (United Kingdom)* 1996, 17/2 (265-269).
11. Teel R.W. Ellagic acid binding to DNA as a possible mechanism for its antimutagenic and anticarcinogenic action. *Cancer Letters (Ireland)* 1986, 30/3 (329-336).
12. Soni K.B, et al. Protective effect of food additives on aflatoxin-induced mutagenicity and hepatocarcinogenicity. *Cancer Letters (Ireland)* 1997, 115/2 (129-133).
13. Dixit R, et al. Inhibition of N-methyl-N-nitrosourea-induced mutagenicity and DNA methylation by ellagic acid. *Proceedings of the National Academy of Sciences of the United States of America (United States)* 1986, 83/21 (8039-8043).
14. Stoner GD, et al. Polyphenols as cancer chemopreventive agents. *J Cell Biochem Suppl* 1995;22:169-80.
15. Teel R.W, et al. Antimutagenic effects of polyphenolic compounds. *Cancer Letters (Ireland)* 1992, 66/2 (107-113).
16. Wilson T, et al. The effect of ellagic acid on xenobiotic metabolism by cytochrome P-450IIE1 and nitrosodimethylamine mutagenicity. *Cancer Letters (Ireland)* 1992, 61/2 (129-134).
17. Narayanan B.A, et al. p53/p21(WAF1/CIP1) expression and its possible role in G1 arrest and apoptosis in ellagic acid treated cancer cells. *Cancer Letters (Ireland)* 1999, 136/2 (215-221).
18. Stoner GD, et al. Lung tumors in strain A mice: application for studies in cancer chemoprevention. *J Cell Biochem Suppl* 1993;17F:95-103.

19. Teel R.W, et al. Ellagic acid metabolism and binding to DNA in organ explant cultures of the rat. *Cancer Letters (Ireland)* 1987, 36/2 (203-211).
20. Stoner GD, et al. Polyphenols as cancer chemopreventive agents. *J Cell Biochem Suppl* 1995;22:169-80.
21. Castonguay A. Pulmonary carcinogenesis and its prevention by dietary polyphenolic compounds. *Ann N Y Acad Sci* 1993 May 28;686:177-85.
22. Stoner G.D, et al. Isothiocyanates and plant polyphenols as inhibitors of lung and esophageal cancer. *Cancer Letters (Ireland)* 1997, 114/1-2 (113-119).
23. Loarca-Pina G, et al. Antimutagenicity of ellagic acid against aflatoxin B₁ in the Salmonella microsuspension assay. *Mutation Research - Environmental Mutagenesis and Related Subjects (Netherlands)* 1996, 360/1 (15-21).
24. Barch D.H, et al. Dietary ellagic acid reduces the esophageal microsomal metabolism of methylbenzyl nitrosamine. *Cancer Letters (Ireland)* 1989, 44/1 (39-44).
25. Castonguay A, et al. Antitumorigenic and antipromoting activities of ellagic acid, ellagitannins and oligomeric anthocyanin and procyanidin. *International Journal of Oncology (Greece)* 1997, 10/2 (367-373).
26. Rao C.V, et al. Chemoprevention of colon carcinogenesis by dietary administration of piroxicam, alpha-difluoromethylornithine, 16alpha-fluoro-5-androsten-17-one, and ellagic acid individually and in combination. *Cancer Research* 1991, 51/17 (4528-4534).
27. Bradlow HL, et al. Phytochemicals as modulators of cancer risk. *Adv Exp Med Biol* 1999;472:207-21.
28. Kelloff GJ, et al. Progress in cancer chemoprevention: development of diet-derived chemopreventive agents. *J Nutr* 2000 Feb;130 (2S Suppl):467S-471S.
29. Wang X, et al. Enhanced cytotoxicity of mitomycin C in human tumour cells with inducers of DT-diaphorase. *Br J Cancer* 1999 Jun;80(8):1223-30.
30. Lee SK, et al. Modulation of in vitro biomarkers of the carcinogenic process by chemopreventive agents. *Anticancer Res* 1999 Jan-Feb;19(1A):35-44.
31. Hecht SS, et al. Chemoprevention of cancer by isothiocyanates, modifiers of carcinogen metabolism. *J Nutr* 1999 Mar;129 (3):768S-774S.
32. Zhang Y, et al. Mechanism of differential potencies of isothiocyanates as inducers of anticarcinogenic Phase 2 enzymes. *Cancer Res* 1998 Oct 15;58(20):4632-9.
33. Kelloff GJ, et al. New agents for cancer chemoprevention. *J Cell Biochem Suppl* 1996;26:1-28.
34. Gamet-Payrastre L, et al. Sulforaphane, a naturally occurring isothiocyanate, induces cell cycle arrest and apoptosis in HT29 human colon cancer cells. *Cancer Res* 2000 Mar 1;60(5):1426-33.
35. Kong AN, et al. Signal transduction events elicited by natural products: role of MAPK and caspase pathways in homeostatic response and induction of apoptosis. *Arch Pharm Res* 2000 Feb;23(1):1-16.
36. Zhang Y. Role of glutathione in the accumulation of anticarcinogenic isothiocyanates and their glutathione conjugates by murine hepatoma cells. *Carcinogenesis* 2000 Jun;21(6):1175-1182.
37. Singletary K, et al. Inhibition of benzo[a]pyrene- and 1,6-dinitropyrene-DNA adduct formation in human mammary epithelial cells by dibenzoylmethane and sulforaphane. *Cancer Lett* 2000 Jul 3;155(1):47-54.
38. Kopelovich L, et al. Progress in cancer chemoprevention. *Ann N Y Acad Sci* 1999;889:1-13.
39. Yu R, et al. p38 mitogen-activated protein kinase negatively regulates the induction of phase II drug-metabolizing enzymes that detoxify carcinogens. *J Biol Chem* 2000 Jan 28;275(4):2322-7.

40. Hirano T, et al. Antiproliferative effects of synthetic and naturally occurring flavonoids on tumor cells of the human breast carcinoma cell line, ZR-75-1. *Res Commun Chem Pathol Pharmacol* 1989 Apr;64(1):69-78.

41. Kuiper GG, et al. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. *Endocrinology* 1998 Oct;139(10):4252-63.

42. Ma JY, et al. A sesquiterpene lactone glucoside from *Ixeris denticulata* f. *pinnatipartita*. *Phytochemistry* 1999 Jan;50(1):113-5.

43. Holland MB, et al. Estrone-induced cell proliferation and differentiation in the mammary gland of the female Noble rat. *Carcinogenesis* 1995 Aug;16(8):1955-61.

44. Wang C, et al. Lignans and flavonoids inhibit aromatase enzyme in human preadipocytes. *J Steroid Biochem Mol Biol* 1994 Aug;50(3-4):205-12.

45. Frank SA, et al. Effects of aging on glucose regulation during wakefulness and sleep. *Am J Physiol* 1995 Dec;269(6 Pt 1):E1006-16.

46. Stout RW. Glucose tolerance and ageing. *J R Soc Med* 1994 Oct;87(10):608-9.

47. Morganti P, et al. Gelatin-cystine, keratogenesis and structure of the hair. *Boll Soc Ital Biol Sper* 1983 Jan 31;59(1):20-5.

48. Hochman L.G, et al. Brittle nails: Response to daily biotin supplementation. *Cutis (United States)* 1993, 51/4 (303-305).

49. Bardazzi F, et al. Biotin in the treatment of idiopathic brittle nails. *Giornale Italiano di Dermatologia e Venereologia (Italy)* 1993, 128/12 (699-702).

50. Zhang H, et al. Biotin administration improves the impaired glucose tolerance of streptozotocin-induced diabetic Wistar rats. *J Nutr Sci Vitaminol (Tokyo)* 1997 Jun;43(3):271-80.

51. Furukawa Y. Enhancement of glucose-induced insulin secretion and modification of glucose metabolism by biotin. [Article in Japanese] *Nippon Rinsho* 1999 Oct;57(10):2261-9.

52. McCarty MF. High-dose biotin, an inducer of glucokinase expression, may synergize with chromium picolinate to enable a definitive nutritional therapy for type II diabetes. *Med Hypotheses* 1999 May;52(5):401-6.

53. Haulica I, et al. Implications of oxidative stress in senescence. [Article in Romanian] *Rev Med Chir Soc Med Nat Iasi* 2000 Apr-Jun;104(2):15-9.

54. Ceconi C, et al. The role of glutathione status in the protection against ischaemic and reperfusion damage: effects of N-acetyl cysteine. *J Mol Cell Cardiol* 1988 Jan;20(1):5-13.

55. Baas P, et al. Effect of N-acetylcysteine on Photofrin-induced skin photosensitivity in patients. *Lasers Surg Med* 1995;16(4):359-67.

56. Urban T, et al. Neutrophil function and glutathione-peroxidase (GSH-px) activity in healthy individuals after treatment with N-acetyl-L-cysteine. *Biomed Pharmacother* 1997;51(9):388-90.

57. Baik HW, et al. Vitamin B12 deficiency in the elderly. *Annu Rev Nutr* 1999;19:357-77.

58. Loew D, et al. Studies on vitamin B12 status in the elderly--prophylactic and therapeutic consequences. *Int J Vitam Nutr Res* 1999 May;69(3):228-33.

59. Bachli E, et al. [Diagnosis of vitamin B12 deficiency: only apparently child's play]. *Schweiz Med Wochenschr* 1999 Jun 12;129(23):861-72.

60. Carr AC, Tijerina T, Frei B. Vitamin C protects against and reverses specific hypochlorous acid- and chloramine-dependent modifications of low-density lipoprotein. *Biochem J* 2000 Mar 1;346 Pt 2:491-9.

61. Romani AM, et al. Regulation of cellular magnesium. *Front Biosci* 2000 Aug 1;5:D720-34.

62. Saatman KE, et al. Acute cytoskeletal alterations and cell death induced by experimental brain injury are attenuated by magnesium treatment and exacerbated by magnesium deficiency. *J Neuropathol Exp Neurol* 2001 Feb;60(2):183-94.
63. Girodon F, et al. Impact of trace elements and vitamin supplementation on immunity and infections in institutionalized elderly patients: a randomized controlled trial. *MIN. VIT.AOX. geriatric network. Arch Intern Med* 1999 Apr 12;159(7):748-54.
64. Brod SA. Unregulated inflammation shortens human functional longevity. *Inflamm Res* 2000 Nov;49(11):561-70.
65. Ward PA. Cytokines, inflammation, and autoimmune diseases. *Hosp Pract (Off Ed)* 1995 May 15;30(5):35-41
66. Rintala RJ, et al. Sodium cromoglycate in the management of chronic or recurrent enterocolitis in patients with Hirschsprung's disease. *J Pediatr Surg* 2001 Jul;36(7):1032-5.
67. Kiechl S, et al. Chronic infections and the risk of carotid atherosclerosis: prospective results from a large population study. *Circulation* 2001 Feb 27;103(8):1064-70.
68. Ip C, et al. Methylselenocysteine modulates proliferation and apoptosis biomarkers in premalignant lesions of the rat mammary gland. *Anticancer Res.* 2001 Mar-Apr;21(2A):863-7.
69. Lu J, et al. Effect on an aqueous extract of selenium-enriched garlic on in vitro markers and in vivo efficacy in cancer prevention. *Carcinogenesis* 1996 Sep;17(9):1903-7.
70. Sinha R, et al. Effects of methylselenocysteine on PKC activity, cdk2 phosphorylation and gadd gene expression in synchronized mouse mammary epithelial tumor cells. *Cancer Lett.* 1999 Nov 15;146(2):135-45.
71. Sinha R, et al. Inhibition of cdk2 kinase activity by methylselenocysteine in synchronized mouse mammary epithelial tumor cells. *Carcinogenesis* 1997 Aug;18(8):1541-7.
72. Yeo JK, et al. Se-methylselenocysteine induces apoptosis through caspase activation and Bax cleavage mediated by calpain in SKOV-3 ovarian cancer cells. *Cancer Lett* 2002 Aug 8;182(1):83-92.
73. Jung U, et al. Se-methylselenocysteine induces apoptosis mediated by reactive oxygen species in HL-60 cells. *Free Radic Biol Med.* 2001 Aug 15;31(4):479-89.
74. Jiang C, et al. Selenium-induced inhibition of angiogenesis in mammary cancer at chemopreventive levels of intake. *Mol Carcinog* 1999 Dec;26(4):213-25.
75. Whanger PD, et al. Tumorigenesis, metabolism, speciation, bioavailability, and tissue deposition of selenium in selenium-enriched ramps (*Allium tricoccum*). *J Agric Food Chem* 2000 Nov;48(11):5723-30.
76. Guo X, et al. Distribution of free seleno-amino acids in plant tissue of *Melilotus indica* L. grown in selenium-laden soils. *Ecotoxicol Environ Saf* 1998 Mar;39(3):207-14.
77. Wang X, et al. Long-term exposure of HL60 cells to 1,25 dihydroxyvitamin D3 reduces their tumorigenicity; a model for cancer chemoprevention. *Proc Soc Exp Biol Med* 1997 Sep;215(4):399-404.
78. van den Bemd GJ, et al. Vitamin D and vitamin D analogs in cancer treatment. *Curr Drug Targets* 2002 Feb;3(1):85-94.
79. Vieth RL. Vitamin D supplementation, 24-hydroxyvitamin D concentrations, and safety. *Am J Clin Nutr* 1999; 69:842-56.

[Back to the Magazine Forum](#)

disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication without first consulting your physician.