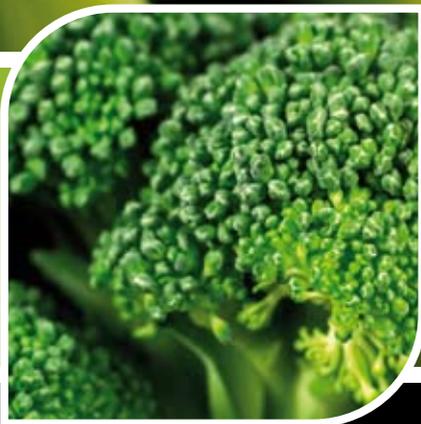
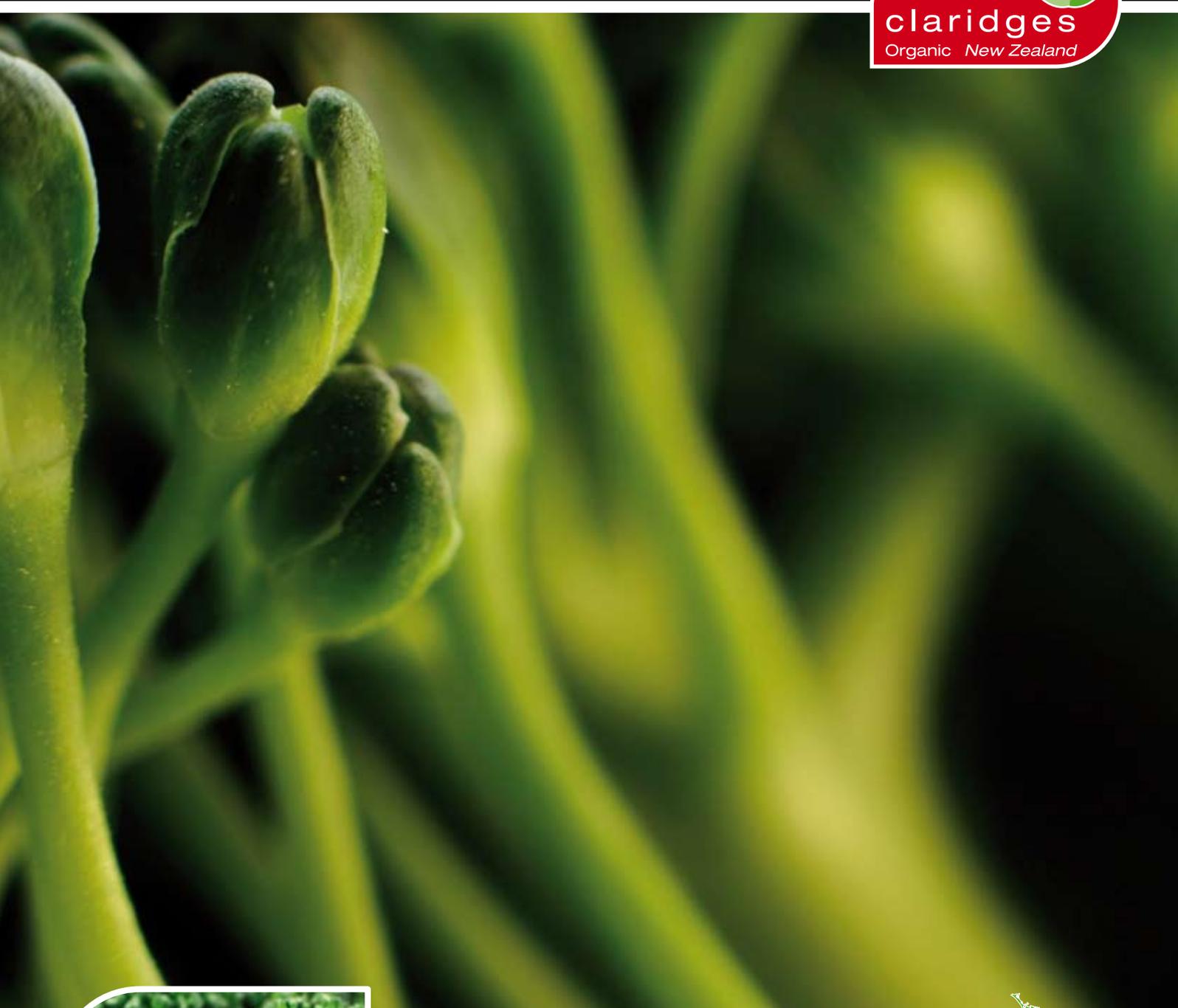




BRINGING ORGANICS TO THE WORLD



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PROTECTIVE EFFECTS OF BROCCOLI / SULFORAPHANE FOR SPECIFIC DISEASES

There are many hundreds of scientific papers reporting the composition and potential health benefits of Brassica vegetables, and even more specifically broccoli. Although broccoli contains a diversity of nutrients and phytochemicals, such as flavonoids and carotenoids, the components that uniquely set crucifers apart from other vegetables are the glucosinolates. Epidemiological data, supported by experimental studies with cell and animal models and more recently small-scale human intervention trials, suggest that broccoli and glucosinolates and their degradation products may have beneficial effects on health. The glucosinolates are modified amino acids, bearing an N-sulfate and an S-glucose moiety. While over 120 side chain structures for glucosinolates have been described, only a restricted number of side chain structures occur in commonly consumed cruciferous crops. Broccoli typically has as its major aliphatic glucosinolate, methionine-derived glucoraphanin (4-methylsulphinylbutyl glucosinolate). When broccoli seeds, sprouts, or the mature vegetable is crushed, the enzyme myrosinase comes into contact with glucoraphanin forming both the isothiocyanate sulforaphane (1-isothiocyanato-4-methylsulfinylbutane) and the related nitrile. Although the nitrile lacks bioactivity at dietary levels sulforaphane is considered by many to be responsible for the major part of cancer prevention by broccoli.

The multiple actions of sulforaphane in humans have been widely studied since 1992 when Prof. Paul Talalay and associates at Johns Hopkins University discovered its action as an inducer of detoxifying enzyme systems. Since then hundreds of scientific papers have been published detailing the effects of sulforaphane on cardiovascular disease, certain forms of cancer, diabetes, and degenerative diseases such

as Alzheimer's and Parkinson's disease. Sulforaphane acts in a number of ways in the human body. Firstly, it stimulates one of the body's natural defence systems (phase II enzymes) which means the body is better able to detoxify and remove potentially harmful chemicals (e.g. carcinogens) that may have been ingested with the meal. This helps to prevent DNA damage caused by carcinogens, thereby preventing tumour formation. Sulforaphane has also been shown to help prevent cancer cell division (tumour growth), cancer cell to cell signalling, angiogenesis and several other processes in the cancer cascade. The strong antioxidant ability of sulforaphane has been shown to reduce inflammation that can lead to heart disease. However, it is important to remember that broccoli contains more than just sulforaphane and these compounds in their own right possess health benefits, but there may also be synergies between the various components.

Below is a summary of the health benefit literature. There are hundreds of papers reporting the potential health benefits of Brassica vegetables and even more specifically broccoli. This report summarises the potential benefits by disease and is adapted from information on the Brassica Protection website (www.brassica.com) with additional and updated information.

CANCER

The evidence shows Brassica vegetable consumption is most strongly associated with a decreased risk of lung, stomach, colon and rectal cancer, and less strongly associated with a decreased risk of cancers of the prostate, ovaries and endometrium (Verhoeven et al. 1996). Several studies of breast and prostate cancer, have given more inconsistent results. There are many factors that could lead to confusing results, including genetic factors, and research continues into this. Below are some of the papers citing results for particular cancers.



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BLADDER CANCER

An epidemiological study shows a strong inverse correlation between cruciferous vegetable consumption and bladder cancer (Tang et al. 2008). The data suggest an increased intake of cruciferous vegetables may reduce the risk of bladder cancer by 36%.

In a joint study, scientists from Roswell Park Cancer Institute, New Zealand Institute for Crop & Food Research Limited, and Johns Hopkins University, found that sulforaphane significantly stimulates phase II enzymes in cultured bladder cells and rat bladder tissue (Zhang et al. 2006). Researchers fed rats a broccoli sprout extract of the isothiocyanate sulforaphane, which is known to induce phase II enzymes. Subsequent urinary output showed dose-dependent high levels of isothiocyanate metabolites with no sign of toxicity. These findings suggest that sulforaphane may be especially effective in protecting against bladder cancer.

A concentrated extract from broccoli sprouts may cut the development of bladder cancer by more than 50%, according to results of an animal study by Munday et al. (2008). Researchers used a freeze-dried aqueous extract of broccoli sprouts that contained approximately 600 times the isothiocyanates content of mature broccoli. Rats were assigned to one of five groups. All groups were fed a control diet for 2 weeks. After a further 2 weeks, three groups were given a bladder cancer-inducing chemical (BBN) in drinking water. Two of these groups were given the broccoli extract in diet (low and high dose), beginning 2 weeks before the carcinogenic chemical was delivered. The two control groups were fed the control diet, while the second received only the broccoli extract to test for safety. At the end of the study, about 96% of animals given only BBN developed an average of almost two tumours each of varying sizes. However, in the animals given BBN and the low dose extract, tumours developed in 22% fewer animals, and the number of tumours per rat was 1.39. Furthermore, animals given BBN and the high dose extract developed about 58% fewer tumours, and

the average number of tumours per animal was only 0.46. In comparison, in both control groups, no tumours developed, and no toxicity from the extract was observed in the animals.

Other papers also indicate beneficial effects for bladder cancer (Li et al. 2005; Tang & Zhang 2004a & b).

BREAST CANCER

The University of California San Diego reports that analysis of data from a multicentre clinical trial involving over 3000 breast cancer survivors suggests that a diet rich in fruit, vegetables and fibre and relatively low in fat showed a risk reduction of cancer recurrence among women who did not experience hot flashes (Gold et al. 2009). The results of the trial indicated women who did not experience hot flashes during early stage breast cancer, and who ate more fruits, vegetables and fibre than the USDA recommended allowance of five servings a day, had a 31% reduction in cancer recurrence over those women who experienced hot flashes and ate the USDA dietary recommendation. Women who had been through menopause had an even lower risk of with a 47% reduction in cancer recurrence.

After rats ingested 150 μ M of sulforaphane, mammary tissue was analysed 30 minutes and 24 hours later for the presence of phase II enzyme induction activity (Cornblatt et al. 2007). Findings confirmed results of past studies and showed significant elevation of phase II enzyme activity. Researchers followed this with a proof of principle pilot study involving eight healthy women undergoing reduction mammoplasty. These women ingested 200 μ M of sulforaphane extract derived from broccoli sprouts an average of 50 minutes before undergoing surgery. Subsequently, epithelial cells removed from breast tissue revealed the presence of phase II enzymatic activity. This demonstrates that there is uptake of sulforaphane in breast tissue following oral administration.

One of the critical factors that determines the capacity of a carcinogen to cause cancer is its ability to bind to DNA. This





carcinogen-DNA binding, or adduct formation, causes DNA mutations when the DNA is replicated during cell division. Most of these mutations are never seen and result in cell death. However, a very small percentage can result in uncontrolled growth that may lead to cancer. In a paper published in *Cancer Letters*, a research group at the University of Illinois showed that sulforaphane significantly reduces the formation of these carcinogen-DNA adducts in human mammary cells (Singletary & MacDonald 2000).

COLON CANCER

A Rutgers study indicated a synergistic relationship between EGCG and sulforaphane (Nair et al. 2008). According to the researchers, “the effects of these two phytochemicals in combination, was dramatically enhanced over the effects of either of the compounds alone, or their additive effects.” The complex molecular interactions and cell signaling pathways make direct translation of the results to human cancers problematic, but the authors suggest that the present study “may point to a singular role for AP-1 mediated transcriptional control of potentially critical genes mediating cancer initiation and progression. This translates into potentially greater efficacy, of the combination of SFN [sulforaphane] and EGCG in chemoprevention of cancer.”

Sulforaphane and DIM, separately, possess growth-inhibiting and cell death-inducing properties in cancer cell lines in vitro (Pappa et al. 2007). In this study, researchers examined the effect of sulforaphane and DIM on human colon cancer cells. The results indicate that at low doses, sulforaphane and DIM fight against each other. However, at higher concentrations, the joint effects grew synergistic. Sulforaphane normally induces phase II enzymes at concentrations of 1–5 μM . When paired with DIM, sulforaphane induced cell death at a minimum of 10 μM . Moreover, at equal concentrations of 10 μM , DIM and sulforaphane together caused stronger cell cycle arrest

than each would do individually. The significance of this study centres on the use of human colon cancer cells instead of animal, and the synergistic effects of the two phytochemicals.

Researchers at the American Health Foundation, Valhalla, NY, showed that sulforaphane significantly inhibited the formation of colon cancer in rats (Chung et al. 2000). These findings provided the first evidence that sulforaphane plays an important role in preventing colon cancer.

LIVER CANCER

In a rural area of China where there is a very high prevalence of liver cancer due to a confluence of hepatitis virus and environmental toxins, scientists from Johns Hopkins University and Qidong Liver Institute PRC near Shanghai performed experiments to measure the ability of broccoli sprouts to increase the body’s abilities to detoxify carcinogens (Kensler et al. 2005). In a single-blinded placebo-controlled trial (100 test, 100 control), subjects drank a hot water extract of 3-day-old broccoli sprouts or a placebo daily for 2 weeks. The subjects’ urine was tested to measure detoxification capacity. The broccoli sprouts test group showed a significant reduction in aflatoxin-DNA adduct levels with increasing levels of broccoli sprout consumption. The change in these biomarkers strongly suggests that there was an enhanced detoxification (neutralisation) of carcinogens from the human body, leading to a reduction in cancer risk.

LUNG CANCER

In the September 15, 2005 issue of *Cancer Research*, scientists from five medical research centers reported that sulforaphane and another isothiocyanate called PEITC could prevent benign tumours produced by a cigarette carcinogen from developing into full-blown cancer tumours in lungs of mice (Conaway et al. 2005). By using a model in which the animals were exposed to the carcinogens before administration of the chemoprotective agent, they demonstrated that the agent (sulforaphane) inhibits



the progression of the disease by reducing proliferation and causing apoptosis – programmed cell death of the damaged cells. These findings suggest that chemoprotective agents might be useful among populations that have already been exposed to tobacco carcinogens. This might be useful, for example, as chemoprotective agents for current smokers, ex-smokers, or those exposed to second-hand smoke.

PANCREATIC CANCER

Chan et al. (2008) demonstrated that the stress-associated hormone, norepinephrine, can increase the cell proliferation and IL-6 levels of human pancreatic duct epithelial cells, which can be inhibited by sulforaphane.

PROSTATE CANCER

In one key study volunteers were randomly assigned to either a broccoli-rich or a pea-rich diet (Traka et al. 2008). After 6 months there were no differences in gene expression between glutathione S-transferase mu 1 (GSTM1) positive and null individuals on the pea-rich diet but significant differences between GSTM1 genotypes on the broccoli-rich diet, associated with transforming growth factor beta 1 (TGFb1) and epidermal growth factor (EGF) signalling pathways. Comparison of biopsies obtained before and after intervention revealed more changes in gene expression occurred in individuals on a broccoli-rich diet than in those on a pea-rich diet. While there were changes in androgen signalling, regardless of diet, men on the broccoli diet had additional changes to mRNA processing, and TGFb1, EGF and insulin signalling. We also provide evidence that sulforaphane (the isothiocyanate derived from 4-methylsulphanylbutyl glucosinolate that accumulates in broccoli) chemically interacts with TGFb1, EGF and insulin peptides to form thio-ureas, and enhances TGFb1/Smad-mediated transcription. These findings suggest that consuming broccoli interacts with GSTM1 genotype to result in complex changes to signalling pathways associated with inflammation and carcinogenesis in the prostate. The authors of that study proposed that these changes may be mediated through the

chemical interaction of isothiocyanates with signalling peptides in the plasma. The study provides, for the first time, experimental evidence obtained in humans to support observational studies that diets rich in cruciferous vegetables may reduce the risk of prostate cancer and other chronic disease.

Human prostate cancer cells responded well to treatment with sulforaphane in the form of broccoli sprout extracts, showing dramatic increases in their phase 2 protective enzymes (Brooks et al. 2001). In an article, Dr. James D. Brooks of the Urology Department at Stanford University suggests that “intervention trials may be warranted [in humans], and broccoli sprouts, a rich natural source of sulforaphane, may be appropriate for use in such a trial.”

Other evidence for a role in prostate cancer prevention comes from papers by Canene-Adams et al. (2007) and Myzak et al. (2007).

SKIN CANCER

A team of Johns Hopkins scientists, lead by Dr. Paul Talalay, applied a broccoli sprout extract to the skin of human volunteers (Talalay et al. 2007). Skin redness and inflammation from UV-ray exposure were noticeably reduced in extract-treated skin. Although the research was conducted on skin, the effect was not that of a sunscreen or sun block but rather the sulforaphane boosts the cellular protective processes in the skin such that it could resist the damage of UV light. In addition, this protection persisted for several days, demonstrating the long lasting antioxidant effect.

In another study from Johns Hopkins, mice were exposed to damaging levels of UV light for a period of 20 weeks (Dinkova-Kostova et al. 2005). Following this, sulforaphane was applied topically to the test group for 11 weeks and compared with untreated controls. At the conclusion of the test, 100% of the control group had tumours. Number of mice with tumors, number of tumours per mouse, and mass of tumours were all reduced by about 50% in the animals that received the broccoli sprout extract.





This protocol mirrors the situation of humans exposed to a great deal of sun during childhood, and lower exposure in later life. The significance of this work is that application of the chemoprotective agent was given after exposure to the carcinogen, thus suggesting its ability to prevent progression to cancer. Further the test was designed to prevent any “sunscreens” effect of the blocking of the UV radiation, thus ensuring that the results could be attributed to the detoxifying protective effects of the broccoli sprout extracts. Thus, topical application of sulforaphane-containing broccoli sprout extracts is a promising strategy for protecting against skin tumour formation after exposure to UV radiation.

ALZHEIMER’S DISEASE

Natural compounds from broccoli possess activity similar to treatments used for symptoms of Alzheimer’s disease (Chiu & Houghton 2005). Acetylcholinesterase (AChE) inhibitors have been used to treat symptoms of Alzheimer’s disease. Peter Houghton and colleagues in the Department of Pharmacy at King’s College London, tested orange, radish, apple, broccoli and potato for this activity and showed that broccoli contains anti-AChE activity. Further they determined that activity appears to be the result of broccoli’s glucosinolate content.

ASTHMA

A study from UCLA shows that sulforaphane triggers an increase of antioxidant enzymes in the human airway that offers protection against free radicals that we breathe in every day in polluted air and pollen (Riedl et al. 2009). Free radicals can cause oxidative tissue damage, which leads to inflammation and respiratory conditions such as asthma. The team fed 65 individuals varying amounts of broccoli sprouts or alfalfa sprouts (which acted as a placebo) for 3 days. Rinses of nasal passages were collected at the beginning and end of the study to evaluate the gene expression of antioxidant enzymes in cells

of the upper airways. Researchers found significant increases of antioxidant enzymes at broccoli sprout doses of 100 g and higher, compared with the placebo group.

BRAIN INJURY

Sulforaphane may help to maintain the integrity of the blood-brain barrier following injury (Zhao et al. 2007). This animal study indicated that sulforaphane increased activity of NF-E2-related factor-2 (Nrf2). Nrf2 binds to the antioxidant response element (ARE), influencing expression of so-called cytoprotective proteins. Sulforaphane treatment of uninjured and brain-injured rats increased cortical expression of Nrf2-driven genes. Tight junction proteins are key to maintaining blood-brain barrier integrity, and they decline after brain injury. Sulforaphane reduced the loss of these proteins as well as the loss of endothelial cells and also reduced the injury-related increase in blood-brain barrier permeability and brain oedema.

CHOLESTEROL

In a pilot study, researchers from the Tokyo University of Agriculture and The Japan Institute for the Control of Ageing found that among individuals who ate 3.5 ounces of broccoli sprouts a day for just 1 week, overall cholesterol levels decreased (Murashima et al. 2004). Participants’ levels of HDL, or “good” cholesterol, increased during this study. The sulforaphane glucosinolate (SGS) in the broccoli sprouts also reduced the amount of oxidative stress, or cell destruction caused by free radicals.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD)

Researchers in the Department of Environmental Health Sciences and the Division of Pulmonary and Critical Care



Medicine at Johns Hopkins School of Medicine report that sulforaphane increases the activity of the phase II enzyme gene NRF2 in human lung cells, which protects cells from damage caused by toxins (Malhotra et al. 2008). This presents the possibility of therapy directed toward enhancing NRF2-regulated antioxidants reducing the effects of oxidative stress in the pathogenesis of COPD.

DIABETES

A study on the effect of sulforaphane on blood vessel cells damaged by hyperglycemia showed a 73% reduction of Reactive Oxygen Species (ROS) molecules (Xue et al. 2008). High glucose levels can cause a three-fold increase in ROS levels, which can damage human cells. Furthermore, the scientists also found that sulforaphane activated the Nrf2 protein, which protects cells and tissues from damage by stimulating the phase 2 enzymes, which detoxify ROS molecules. These results suggest that sulforaphane from broccoli may help reverse the damaging effects of diabetes-linked vascular disease.

HEART DISEASE

Intake of cruciferous vegetables is inversely related to serum homocysteine levels, a risk factor for heart disease, suggesting that cruciferous vegetables may offer protection from heart disease (Tucker et al. 1996; Ganji & Kafai 2004). However, two out of three epidemiological studies of diet and risk of heart disease failed to find a relationship between crucifer intake and risk of heart attack (Hung et al. 2004; Genkinger et al. 2004). The third, more recent study considered the possibility that, like the effect of crucifers on risk of cancer, polymorphism in GSTs might confound the issue (see Traka & Mithen 2008 for a discussion of GST polymorphism, crucifers and cancer risk).

A research team at the Cardiovascular Research Center, University of Connecticut School of Medicine in the US published a laboratory study in the scientific journal *The Journal of Agricultural and Food Chemistry* (Mukherjee et al. 2007). One group of rats was fed liquified broccoli and six control animals were fed only water. After 30 days, the researchers simulated a heart attack in the animals by removing the hearts and cutting off the blood supply for 30 minutes, followed by 2 hours where the blood flow was returned. Compared with the control group, the rats fed broccoli showed improved heart muscle function after the experimental heart attack: they had a smaller amount of dead heart muscle and heart muscle cells. These changes were accompanied by changes in several proteins found in the cell nuclei, and other chemicals thought to protect the heart. The scientists consider that selenium and glucosinolates play an important role in improved heart function.

HYPERTENSION

Dr. Bernhard Juurlink at the University of Saskatchewan, in Saskatoon, Canada, found that sulforaphane fed to rats with high blood pressure improved cardiovascular health by decreasing inflammation and improving heart, arteries and kidney function (Wu et al. 2004). According to Dr. Juurlink proves that the antioxidant can correct damage already done to the cardiovascular system.

Other evidence for benefits for cardiovascular health comes from papers by Noyan-Ashraf et al. (2006) and Wu & Juurlink (2001).

IMMUNITY

Kim et al. (2008) showed that direct administration of sulforaphane in broccoli reversed the decline in cellular immune function in old mice, and similar results were shown in individual immune cells from old mice, treated with the





chemical outside the body and then placed back into a recipient animal. Dendritic cells, which introduce infectious agents and foreign substances to the immune system, were particularly effective in restoring immune function in aged animals when treated with sulforaphane. To investigate how the chemical in broccoli increased the immune system's response, the UCLA group confirmed that sulforaphane interacts with a protein called Nrf2, which serves as a master regulator of the body's overall antioxidant response and is capable of switching on hundreds of antioxidant and rejuvenating genes and enzymes. The researchers found that although there is a decline in Nrf2 activity with aging, this pathway remains accessible to chemicals like sulforaphane that are capable of restoring some of the ravages of ageing by boosting antioxidant pathways.

JOINT INFLAMMATION

Sulforaphane appears to block enzymes that trigger inflammation in joints (Healy et al. 2005). A team at Johns Hopkins University added sulforaphane to cartilage cells from human joints. After 24 hours, the cells were subjected to stress tests. The sulforaphane boosted phase 2 enzymes that prevented the activation of the systems that trigger inflammation. In addition, sulforaphane prevented apoptosis (programmed cell death). Zachary Healy, the lead author of the paper published in the Proceedings of the National Academy of Science, USA, suggests that although much work would need to be done to confirm this effect in humans, these natural dietary compounds have the potential to stop pain and inflammation before they start and ideally might be used prior to sporting activities.

LIVER

Oral administration of sulfur-radish extract and of sulforaphane after CCl4-induced liver injury both decreased the serum level of ALT, reduced the necrotic zones, inhibited lipid peroxidation,

and induced phase 2 enzymes without affecting cytochrome P450-2E1 (CYP2E1) (Baek et al. 2008). These results suggest that the administration of the sulfur-radish extract and of sulforaphane may partially prevent CCl4-induced hepatotoxicity, possibly by indirectly acting as an antioxidant by improving the detoxification system.

PARKINSON'S DISEASE

Parkinson's disease is a progressive disorder resulting from the loss of cells in a section of the brain called the substantia nigra. Those cells produce the neurotransmitter dopamine. Loss of dopamine causes critical nerve cells in the brain to fire uncontrollably, leaving a person unable to direct or control their muscle movement. Preliminary results from in vitro experiments by researchers in Seoul, Korea, indicated that sulforaphane protected dopaminergic cells from the cytotoxicity of 6-OHDA and BH4, compounds known to produce dopamine quinone products and oxidative stress, and to cause selective death of dopaminergic cells (Han et al. 2007). Further studies need to be conducted to determine whether sulforaphane crosses the blood-brain barrier and the amount of dietary intake needed to be effective.

PROTECTION AGAINST POLLUTION

Although sulforaphane's anti-cancer properties are being extensively examined, Ritz et al. (2007) focused on sulforaphane's anti-inflammatory properties and the prevention of pollutant-related respiratory and cardiovascular conditions. Airway inflammation can lead to acute and chronic lung dysfunction, and can also cause systemic responses in the cardiovascular system, affecting blood coagulation and gas exchange. Moreover, oxidative stress results from exposure to air



pollutants as well as from airway inflammation due to disorders such as asthma and COPD. The researchers administered up to 6.25 μM of sulforaphane to human bronchial epithelial tissue *in vitro* to stimulate phase II enzyme induction. The tissue was then subjected to diesel exhaust particles, which resulted in the production of pro-inflammatory cytokines. Tissues that were pretreated with sulforaphane suffered less oxidative stress than control cells that weren't treated. While research needs to proceed *in vivo*, this study suggests preventive properties of sulforaphane on airway tissue damaged by diesel pollutants.

STOMACH

A Johns Hopkins University research team led by Dr. Jed Fahey discovered that sulforaphane kills *H. pylori*, the bacterium responsible for the vast majority of stomach ulcers and stomach cancers, a leading cause of cancer death worldwide (Fahey et al. 2002). In their laboratory experiments, the scientists discovered that purified sulforaphane even killed *Helicobacter* that was resistant to commonly-used antibiotics. They also showed that sulforaphane can kill the bacterium whether it is inside or outside cells. In humans, cells lining the stomach can act as reservoirs of *Helicobacter*, making it more difficult to eradicate the infection. Though the pure compound kills *Helicobacter* efficiently, a number of studies are underway to determine whether dietary sources of sulforaphane (broccoli or broccoli sprouts, for instance) have similar effects.

In a study from Japan, broccoli sprouts were fed to patients infected with *Helicobacter pylori* bacteria. *H. pylori* infection can cause stomach ulcers and markedly increases the risk of developing stomach cancer (Yanaka et al. 2005). After eating 100 g broccoli sprouts daily for 2 months, measures of *H. pylori* infection were substantially reduced. Control subjects fed a vegetable with no sulforaphane or related compounds showed no change, suggesting strongly that the content of SGS in broccoli sprouts caused the reduction of the bacteria.

This confirms test-tube (Fahey et al. 2002) and rodent studies, and a preliminary clinical study (Galan et al. 2004) on the potent and selective antibacterial properties of sulforaphane and its ability to selectively target the *H. pylori* bacteria, which are often difficult to eradicate. "These data strongly suggest that a diet rich in sulforaphane glucosinolate may help protect against gastric cancer, presumably by activating gastric mucosal antioxidant enzymes that can protect the cells from *H. pylori*-induced DNA damage," stated Dr. Akinori Yanaka of the University of Tsukuba, lead author of the Japanese study.

STROKE

A study from the University of Texas Medical Center, published in *Neuroscience Letters*, found that sulforaphane was able to enter a rat's brain and if administered 15 minutes after focal ischemia (local interruption of the blood supply to the brain that mimics strokes), sulforaphane significantly reduced the size of cerebral damage, which is a measure of stroke damage (Zhao et al. 2005). The authors suggested that sulforaphane could offer several advantages as a therapeutic agent, as it can boost several enzymes involved in cellular defense, allowing it to act at multiple targets and also due to its long-lasting activity, might reduce the need for multiple dosages.

VISION

Dr. Paul Talalay and his colleagues at Johns Hopkins University have discovered that sulforaphane boosts the level of a key enzyme that protects the eye from damage caused by UV light (Gao & Talalay 2004). That damage can lead to macular degeneration, the leading cause of blindness among the elderly. Benefits for vision have also been demonstrated by Tanito et al. (2005) and Cano et al. (2008).





REFERENCES

- Baek S-H, Park M, Suh J-H, Choi H-S 2008. Protective Effects of an Extract of Young Radish (*Raphanus sativus* L) Cultivated with Sulfur (Sulfur-Radish Extract) and of Sulforaphane on Carbon Tetrachloride-Induced Hepatotoxicity. *Bioscience, Biotechnology, and Biochemistry* 72(5): 1176-1182.
- Brooks JD, Paton VG, Vidanes G 2001. Potent Induction of Phase 2 Enzymes in Human Prostate Cells by Sulforaphane. *Cancer Epidemiology, Biomarkers & Prevention* 10: 949-954.
- Canene-Adams K, Lindshield BL, Wang S, Jeffery EH, Clinton SK, Erdman JW Jr. 2007. Combinations of tomato and broccoli enhance antitumor activity in dunning r3327-h prostate adenocarcinomas. *Cancer Research* 67(2): 836-843.
- Cano MD, Reyes JM, Park CY, Gao X, Mori K, Chuck RS, Gehlbach PL 2008. Demonstration by redox fluorometry that sulforaphane protects retinal pigment epithelial cells against oxidative stress. *Investigative Ophthalmology & Visual Science* 49(6): 2606-2612.
- Chan C, Lin HJ, Lin J 2008. Stress-associated hormone, norepinephrine, increases proliferation and IL-6 levels of human pancreatic duct epithelial cells and can be inhibited by the dietary agent, sulforaphane. *International Journal of Oncology* 33(2): 415-419.
- Chiu B, Houghton P 2005. Investigation of Common Vegetables for Cholinesterase Inhibitory Activity. *British Pharmaceutical Conference*, 142nd, 9/26-28/2005, p151.
- Chung F-L, Conaway CC, Rao CV, Reddy BS 2000. Chemoprevention of colonic aberrant crypt foci in Fischer rats by sulforaphane and phenethyl isothiocyanate. *Carcinogenesis* 21(12): 2287-2291
- Conaway C, Wang C-X, Pittman B, Yang Y-M, Schwartz J, Tian D, McIntee E, Hecht S, Chung F-L 2005. Phenethyl Isothiocyanate and Sulforaphane and their N-Acetylcysteine Conjugates Inhibit Malignant Progression of Lung Adenomas Induced by Tobacco Carcinogens in A/J Mice. *Cancer Research* 65: 8548-8557.
- Cornblatt BS, Ye L, Dinkova-Kostova AT, Erb M, Fahey JW, Singh NK, Chen T, Stierer M-SA, Garrett-Mayer E, Argani P, Davidson NE, Talalay P, Kensler PW, Visvanathan K 2007. Preclinical and clinical evaluation of sulforaphane for chemoprevention in the breast. *Carcinogenesis* 28: 1485-1490.
- Dinkova-Kostova A, Jenkins S, Fahey J, Ye L, Wehage S, Liby K, Stephenson K, Wade K, Talalay P 2005. Protection against UV-light-induced skin carcinogenesis in SKH-1 high-risk mice by sulforaphane-containing broccoli sprout extracts. *Cancer Epidemiology, Biomarkers & Prevention* 14(11): 243-252.
- Fahey JW, Haristoy X, Dolan PM, Kensler TW, Scholtus I, Stephenson KK, Talalay P, Lozniewski A 2002. Sulforaphane inhibits extracellular, intracellular, and antibiotic-resistant strains of *Helicobacter pylori* and prevents benzo[a]pyrene-induced stomach tumours. *Proceedings of the National Academy of Sciences USA* 99(11): 7610-7615.
- Galan MV, Kishan AA, Silverman AL 2004. Oral Broccoli Sprouts for the Treatment of *Helicobacter pylori* Infection: A Preliminary Report. *Digestive Diseases and Sciences* 49(7/8): 1088-1090.
- Ganji V, Kafai MR 2004. Frequent consumption of milk, yogurt, cold breakfast cereals, peppers, and cruciferous vegetables and intakes of dietary folate and riboflavin but not vitamins B-12 and B-6 are inversely associated with serum total homocysteine concentrations in the US population. *American Journal of Clinical Nutrition* 80:1500-1507.
- Gao X, Talalay P. 2004. Induction of phase 2 genes by sulforaphane protects retinal pigment epithelial cells against photooxidative damage. *Proceedings of the National Academy of Sciences USA* 101(28): 10446-10451.
- Genkinger JM, Platz EA, Hoffman SC, Comstock GW, Helzlsouer KJ 2004. Fruit, vegetable, and antioxidant intake and all-cause, cancer, and cardiovascular disease mortality in a community-dwelling population in Washington County, Maryland. *American Journal of Epidemiology* 160: 1223-1233.
- Gold EB, Pierce JP, Natarajan L, Stefanick ML, Laughlin GA, Caan BJ, Flatt SW, Emond JA, Saquib N, Madlensky L, Kealey S, Wasserman L, Thomson CA, Rock CL, Parker BA, Karanja N, Jones V, Hajek RA, Pu M, Mortimer JE 2009. Dietary pattern influences breast cancer prognosis in women without hot flashes: the women's healthy eating and living trial. *Journal of Clinical Oncology* 27(3): 352-359.
- Han JM, Lee YJ, Lee SY, Kim EM, Moon Y, Kim HW, Hwang O 2007. Protective Effect of Sulforaphane against Dopaminergic Cell Death. *Journal of Pharmacology and Experimental Therapeutics* 321(1): 249-256.
- Healy Z, Lee N, Gao X, Goldring M, Talalay P, Kensler T, Konstantopoulos K 2005. Divergent responses of chondrocytes and endothelial cells to shear stress: Cross-talk among COX-2, the phase 2 response, and apoptosis. *Proceedings of the National Academy of Sciences USA* 102(39): 10410-10415.
- Hung H-C, Joshupura KJ, Jiang R 2004. Fruit and vegetable intake and risk of major chronic disease. *Journal of the National Cancer Institute* 96: 1577-1584.
- Kensler TW, Chen JG, Egner PA, Fahey JW, Jacobson LP, Stephenson KK, Ye L, Coady JL, Wang J-B, Wu Y, Sun Y, Zhang Q-N, Zhang B-C, Zhu Y-R, Qian G-S, Carmella SG, Hecht SS, Benning L, Gange SJ, Groopman JD, Talalay P 2005. Effects of glucosinolate-rich broccoli sprouts on urinary levels of aflatoxin-DNA adducts and phenanthrene tetraols in a randomised clinical study in He Zuo township, Qidong, Peoples Republic of China. *Cancer Epidemiology, Biomarkers & Prevention* 14: 2605-2613.
- Kim H-J, Barajas B, Wang M, Nel AE 2008. Nrf2 activation by sulforaphane restores the age-related decline of Th1 immunity: Role of dendritic cells. *Journal of Allergy and Clinical Immunology* 121(5): 1255-1261.
- Li J, Yao S, Zhang Y 2005. The role of c-Jun in the AP-1 activation induced by naturally occurring isothiocyanates. *Food and Chemical Toxicology* 43(9): 1373-1380.
- Malhotra D, Thimmulappa R, Navas-Acien A, Sandford A, Elliott M, Singh A, Chen L, Zhuang X, Hogg J, Pare P, Tuder RM, Biswal S. 2008. Decline in NRF2-regulated antioxidants in chronic obstructive pulmonary disease lungs due to loss of its positive regulator, DJ-1. *American Journal of Respiratory and Critical Care Medicine* 178(6): 592-604.



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Mukherjee S, Gangopadhyay H, Das DK 2007. Broccoli: A Unique Vegetable That Protects Mammalian Hearts through the Redox Cycling of the Thioredoxin Superfamily. *Journal of Agricultural and Food Chemistry* 56 (2): 609-617.

Munday R, Mhaweche-Fauceglia P, Munday CM, Paonessa JD, Tang L, Munday JS, Lister C, Wilson P, Fahey JW, Davis W, Zhang Y 2008. Inhibition of Urinary Bladder Carcinogenesis by Broccoli Sprouts. *Cancer Research* 68(5): 1593-1600.

Murashima M, Watanabe S, Zhuo X-G, Uehara M, Kurashige A 2004. Phase 1 study of multiple biomarkers for metabolism and oxidative stress after one-week intake of broccoli sprouts. *BioFactors* 22: 271-275.

Myzak MC, Tong P, Dashwood WM, Dashwood RH, Ho E 2007. Sulforaphane retards the growth of human pc-3 xenografts and inhibits hdac activity in human subjects. *Experimental Biology and Medicine* (Maywood) 232: 227-234.

Nair S, Hebbar V, Shen G, Gopalakrishnan V, Oo Khor T, Yu S, Xu C, Kong AN 2008. Synergistic effects of a combination of dietary factors sulforaphane and (-) epigallocatechin-3-gallate in HT-29 AP-1 human colon cancer cells. *Pharmaceutical Research* 25(2): 387-399.

Noyan-Ashraf MH, Wu L, Wang R, Juurlink BHJ 2006. Dietary approaches to positively influence fetal determinants of adult health. *FASEB Journal* 20(2): 371-373.

Pappa G, Strathmann J, Lowinger M, Bartsch H, Gerhauser C 2007. Quantitative combination effects between sulforaphane and 3,3'-diindolylmethane on proliferation of human colon cancer cells in vitro. *Carcinogenesis* 28(7): 1471-1477.

Riedl MA, Saxon A, Diaz-Sanchez, D 2009. Oral sulforaphane increases Phase II antioxidant enzymes in the human upper airway. *Clinical Immunology* 130(3): 244-251.

Ritz SA, Wan J, Diaz-Sanchez D. 2007. Sulforaphane-stimulated phase II enzyme induction inhibits cytokine production by airway epithelial cells stimulated with diesel extract. *American Journal of Physiology - Lung Cellular and Molecular Physiology* 292: L33-L39.

Singletary K, MacDonald C 2000. Inhibition of benzo[a]pyrene- and 1,6-dinitropyrene-DNA adduct formation in human mammary epithelial cells by dibenzoylmethane and sulforaphane. *Cancer Letters* 155(1): 47-54.

Talalay P, Fahey JW, Healy ZR, Wehage SL, Benedict AL, Min C, Dinkova-Kostova AT 2007. Sulforaphane mobilizes cellular defenses that protect skin against damage by UV radiation. *Proceedings of the National Academy of Sciences USA* 104(44): 17500-17505.

Tang L, Zhang Y 2004a. Dietary isothiocyanates inhibit the growth of human bladder carcinoma cells. *Journal of Nutrition* 134(8): 2004-2010.

Tang L, Zhang Y 2004b. Isothiocyanates in the chemoprevention of bladder cancer. *Current Drug Metabolism* 5(2): 193-201.

Tang L, Zirpoli GR, Guru K, Moysich KB, Zhang Y, Ambrosone CB, McCann SE 2008: Consumption of Raw Cruciferous Vegetables is Inversely Associated with Bladder Cancer Risk. *Cancer Epidemiology Biomarkers &*

Prevention 17: 938-944.

Tanito M, Masutani H, Kim Y-C, Nishikawa M, Ohira A, Yodoi J 2005. Sulforaphane Induces Thioredoxin through the Antioxidant-Responsive Element and Attenuates Retinal Light Damage in Mice. *Investigative Ophthalmology & Visual Science* 46(3): 979-987.

Traka M, Gasper AV, Melchini A, Bacon JR, Needs PW, Frost V, Chantry A, Jones AME, Ortori CA, Barrett DA, Ball RY, Mills RD, Mithen RF 2008. Broccoli Consumption Interacts with GSTM1 to Perturb Oncogenic Signalling Pathways in the Prostate. *PLoS ONE* 3(7): e2568.

Traka M, Mithen R 2009. Glucosinolates, isothiocyanates and human health. *Phytochemistry Reviews* 8: 269-282.

Tucker KL, Selhub J, Wilson PW, Rosenberg IH 1996. Dietary pattern related to plasma folate and homocysteine concentrations in the Framingham Heart Study. *Journal of Nutrition* 126: 3025-3031.

Verhoeven DT, Goldbohm RA, van Poppel G, Verhagen H, van den Brandt PA 1996. Epidemiological studies on Brassica vegetables and cancer risk. *Cancer Epidemiology, Biomarkers & Prevention* 5: 733-748.

Wu L, Ashraf MHN, Facci M, Wang R, Paterson PG, Ferrie A, Juurlink BHJ 2004. Dietary approach to attenuate oxidative stress, hypertension, and inflammation in the cardiovascular system. *Proceedings of the National Academy of Sciences USA* 101(18): 7094-7099.

Wu L, Juurlink BHJ 2001. The impaired glutathione system and its up-regulation by sulforaphane in vascular smooth muscle cells from spontaneously hypertensive rats. *Journal of Hypertension* 19(10): 1819-1825.

Xue M, Qian Q, Antonysunil A, Rabbani N, Babaei-Jadidi R, Thornalley PJ 2008. Activation of NF-E2-related factor-2 reverses biochemical dysfunction of endothelial cells induced by hyperglycemia linked to vascular disease. *Diabetes* 57: 2809-2817.

Yanaka A, Zhang S, Yamamoto M, Fahey J 2005. Daily Intake of Sulforaphane-Rich Broccoli Sprouts Improves Gastritis in H.pylori-Infected Human Subjects. *Cancer Epidemiology, Biomarkers & Prevention* 14(11 Part 2): 2754s.

Zhang Y, Munday R, Jobson HE, Munday CM, Lister C, Wilson P, Fahey JW, Mhaweche-Fauceglia P 2006. Induction of GST and NQO1 in cultured bladder cells and in the urinary bladders of rats by an extract of broccoli (*Brassica oleracea italica*) sprouts. *Journal of Agricultural and Food Chemistry* 54(25): 9370-9376.

Zhao J, Kobori N, Aronowski J, Dash PK 2005. Sulforaphane reduces infarct volume following focal cerebral ischemia in rodents. *Neuroscience Letters* 393(2-3): 108-112.

Zhao J, Moore AN, Redell JB, Dash PK 2007. Enhancing expression of Nrf2-driven genes protects the blood-brain barrier after brain injury. *The Journal of Neuroscience* 27(38): 10240-10248.





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