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1. Selenium inhibits angiogenesis in breast cancer

Full source: *Mol Carcinogen* 99, Vol. 26, Iss. 4, Pgs. 213-225

The trace element nutrient selenium (Se) has been shown to possess cancer-preventive activity in both animals and humans. The process of angiogenesis (development of new blood vessels) is necessary for the genesis and growth of solid cancers. A study examined if selenium exerts its cancer-preventive activity, by inhibiting cancer-associated angiogenesis. Increased selenium intake as selenium-enriched garlic, sodium selenite, or Se-methylselenocysteine led to a significant reduction of tumor density in breast cancers during continuous exposure for 7 weeks.

Also, there were significantly lower levels of vascular endothelial cell growth factor activity in a sizeable proportion of the selenium-treated cancers, compared to the control group. In contrast to the breast cancers, the microvessel density of the mammary glands that were not involved, was not altered by the selenium treatment. In cell culture, direct exposure of human umbilical vein endothelial cells to selenium induced cell death predominantly through apoptosis. The results indicate a potential for selenium metabolites to inhibit key attributes (proliferation, survival, and cell matrix degradation) of endothelial cells which are critical for angiogenesis to begin. Therefore, inhibition of angiogenesis associated with cancer may be a mechanism for the anticancer activity of selenium in vivo.

2. DHEA inhibits carcinogen-activating enzyme

Full source: *J Biol Chem* 99, Vol. 274, Iss. 49, Pgs. 35186-35190

The adrenal steroid hormone dehydroepiandrosterone (DHEA) is a potent inhibitor of breast cancer. A study looked at the effect of DHEA on the activation of the carcinogen-activating enzyme cytochrome P450 in human breast cancer cells. Results showed that DHEA inhibited the increase in the enzyme activity that occurs when breast cells are exposed to a known carcinogen. DHEA caused a time- and concentration-dependent decrease in enzyme mRNA levels, indicating that DHEA inhibits the enzyme's activity by decreasing its stability. This demonstrates that DHEA inhibits artificially-induced cytochrome P450 expression and enzyme activity in vitro. Regulating the activity of carcinogen-activating enzymes may be the reason for DHEA's chemopreventive activity.

3. Ginkgo biloba extract and peripheral arterial occlusive disease

Full source: *Arzneim Forsch Drug Res* 99, Vol. 49, Iss. 11, Pgs. 900-904

Several clinical trials have demonstrated the efficacy of Ginkgo biloba extract in the treatment of peripheral arterial occlusive disease. A study that was conducted to confirm the superiority of the higher dosage of Ginkgo biloba extract on 74 individuals indicated the superiority of 240 mg Ginkgo biloba extract daily compared with the standard dosage of 120 mg to 160 mg daily. The primary efficacy criterion was the difference of the pain-free walking distance between the start of treatment and after 24 weeks measured on a treadmill under standardized conditions. The pain-free walking distance improved in both groups. There was a mean increase of 60.6 m in the group who received 120 mg Ginkgo biloba extract daily and a statistically significant higher mean increase of 107.0 m in the group who were treated with the higher dosage. Both dosage regimens investigated in this study led to an improvement of the pain-free walking distance after 24 weeks of treatment. The superiority of the higher dosage over the standard dosage was statistically significant. Both treatment variations were safe and well tolerated.

4. Pattern of alcohol drinking and progression of atherosclerosis

Full source: *Arterioscler Thromb Vasc Biol* 99, Vol. 19, Iss. 12, Pgs. 3001-3006

Most studies that examine the role of alcohol consumption in atherosclerosis and cardiovascular disease have overlooked the possible effect of drinking pattern. A study investigated the association between the habit of heavy acute intake of beer and spirits (bingeing) and the 4-year progression of carotid atherosclerosis in 1635 middle-aged Finnish men. Changes were estimated in maximum and mean intima-media thickness (IMT) and the maximum plaque height. After adjustment for age, baseline carotid atherosclerosis, and average weekly alcohol consumption level, the highest atherosclerosis progression in men was observed for those who usually consumed a whole bottle of vodka or more in 1 session. For beer bingeing (>6 beers at a time), the magnitude of IMT progression was even higher, although this association was only marginally significant because of smaller numbers. The associations were largely unaffected by adjustments for blood pressure, lipids, smoking, BMI, and medication. The magnitude of the difference was generally higher in a subgroup that was free of ischemic heart disease (IHD) at baseline. Thus, the pattern of drinking is associated with the progression of carotid atherosclerosis independently of the total level of alcohol consumption and risk factors.

5. Curcumin inhibits colon cancer cell proliferation

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3675-3680

A study showed that curcumin inhibited cancer cell growth in a dose-dependent manner: Curcumin depressed the ability of special Love cells to form colonies and showed that curcumin was cytotoxic to these cells. The Love cells treated with curcumin mostly stayed in the G(2) growth phase, which prevented cells from entering the next cell growth cycle, thus inducing apoptotic cell death.

6. Health benefits of rice bran oil

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3651-3657

In Asian countries, the relatively high content of the non-fatty acid components of rice bran oil (RBO) are known to have beneficial health effects. Components that are specific to (RBO) are gamma-oryzanol and tocotrienols. (RBO) lowers cholesterol better than more commonly used vegetable oils. In addition, blending RBO with safflower oil, but not with sunflower oil, may magnify the cholesterol-lowering efficacy.

7. Vitamin E protects against liver damage

Full source: *Cell Biochem Funct* 99, Vol. 17, Iss. 4, Pgs. 253-259

A study investigated whether the increase of vitamin E in the liver, influences chronic liver damage induced by carbon tetrachloride (CCl₄) in rats. (Its vapors can depress central nervous system activity and cause degeneration of the liver and kidneys). Rats were divided into three groups: 1) Control 2) given CCl₄ in olive oil and 3) given vitamin E (dl-alpha-tocopherol acetate, 100 mg kg⁻¹). This was administered three times per week for five weeks. Results showed that dangerously higher blood levels of several key enzymes were recorded in animals treated with CCl₄ than in the controls, but had returned to normal values by the administration of vitamin E + CCl₄. Liver vitamin E levels were significantly lower in the CCl₄ group than in the control group. However, the liver vitamin E content was significantly increased in the vitamin E + CCl₄ group. Animals given Vitamin E showed incomplete, but significant, prevention of liver necrosis (cell death) and cirrhosis (inflammation) induced by CCl₄. This indicates that vitamin E has protective effects against CCl₄-induced chronic liver damage and cirrhosis.

8. DHEA treatment for those HIV+

Full source: *Psychoneuroendocrinology* 2000, Vol. 25, Iss. 1, Pgs. 53-68

A study evaluated the effect of dehydroepiandrosterone (DHEA) on depressed mood and fatigue in 45 HIV+ men and women. Additional evaluations were concerned with treatment effects on libido and body cell mass; on serum testosterone levels, and elicitation of short-term side effects. Treatment consisted of an open-label 8-week trial using DHEA doses from 200 to 500 mg/day. Mood was much improved in 72%, and 81% with respect to fatigue. Body cell mass and libido increased significantly by week 8. DHEA therapy did not have an effect on CD4 cell count or on blood testosterone levels in men. DHEA may be a promising treatment for HIV+ patients with depressed mood and fatigue.

9. Green tea extract decreases iron-induced free radical damage

Full source: *J Nutr* 99, Vol. 129, Iss. 12, Pgs. 2130-2134

Regular tea consumption has been associated with a reduced risk of cancer. Green tea contains catechins with antioxidant properties. In one study, cells grown with or without green tea extract were treated with iron as an oxidative stimulus for 2 hours. Supplementation with green tea extract significantly decreased malondialdehyde production and DNA damage after iron oxidative treatment. (Malondialdehyde is a lipid peroxidation product, believed to be a marker of radical generation and tissue damage). In cells untreated with green tea, there was no effect on membrane distribution of (n-3) fatty acids due to iron treatment. It is likely that the protective effects can be attributed to epigallocatechin gallate, which is present mainly (670 g/kg) in green tea extract. This supports a protective effect of green tea against free radical damage.

10. Conjugated linoleic acid (CLA) reduces breast cancer risk in animals

Full source: *J Nutr* 99, Vol. 129, Iss. 12, Pgs. 2135-2142

Conjugated linoleic acid (CLA) is a potent cancer preventive agent in animals. To date, all of the in vivo work with CLA has been done with a commercial free fatty acid preparation containing a mixture of different forms (isomers) of CLA. A study tried to determine whether a high CLA butter fat has biological activities similar to those of the mixture of free fatty acid CLA isomers. Among other variables, the proliferative activity of TEE (terminal end endothelial) cells was evaluated. (It should be

noted that TEE cells are the target cells for breast chemical carcinogenesis). Feeding butter fat CLA to rats during the time of pubescent mammary gland development reduced mammary epithelial mass by 22%, decreased the size of the TEE population by 30%, suppressed the proliferation of TEE cells by 30% and inhibited mammary tumor yield by 53%! All of the other variables responded with the same magnitude of change to both butter fat CLA and the mixture of CLA isomers at the level of CLA (0.8%) present in the diet. Rats consuming the CLA-enriched butter fat also consistently accumulated more total CLA in the mammary gland and other tissues (four- to sixfold increases) compared with those consuming free fatty acid CLA (threefold increases) at the same dietary level of intake. The availability of vaccenic acid in butter fat may serve as the precursor for the endogenous synthesis of CLA. Further studies will be conducted to investigate other attributes of this novel dairy product.

11. **Alcohol consumption and cancer mortality**

Full source: *Amer J Epidemiol* 99, Vol. 150, Iss. 11, Pgs. 1201-1207

A study examined the association between alcohol consumption and mortality in Japan, where mortality and lifestyle differ substantially from Western countries. After excluding subjects with self-reported serious diseases at the start, 19,231 men aged 40-59 years who reported their alcohol intake were followed from 1990-1996, and 548 deaths were documented. The lowest risk was for men who consumed 1-149 g/week (relative risk = 36%), while the highest risk was seen for men who consumed greater than or equal to 450 g/week (relative risk = 168%). The association was modified by smoking, and beneficial effects of moderate drinking were largely limited to nonsmokers. The risk of cancer death showed a similar trend, but increased more in heavy drinkers. The personal background characteristics of the moderate drinkers were healthier than either nondrinkers or heavy drinkers. Thus, moderate alcohol consumption was associated with the lowest risks of all-cause and cancer mortality, especially among nonsmokers.

12. **Chemoprevention of lung cancer by IP6 derivative**

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3659-3661

Myo-inositol is largely formed by the dephosphorylation of inositol hexaphosphate (IP6, phytate) within the gastrointestinal tract in humans and animals. Myo-inositol is one of a relatively few compounds that has an inhibitor effect on development of lung cancer in experimental animals when given during the post-initiation period. It prevents pulmonary adenoma formation in mice when fed the diet after administrations of carcinogens to the mice. A second compound, dexamethasone, also prevents pulmonary neoplasia (progressive multiplication of cells) under the same conditions. Experiments in which both myo-inositol and dexamethasone were administered together in the diet showed an additive inhibitory effect. The significance and utility of the chemopreventive properties of these agents remains to be determined.

13. **IP6 inhibits breast cancer**

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3671-3674

Recent studies show that as the intake of high fiber cereal diets increase, breast cancer rates fall. Inositol hexaphosphate (IP6) is abundant in cereals, legumes, and seeds. Experiments demonstrate a reproducible and striking anti-cancer action of IP6. It therefore appears that IP6 is one of the components, if not the most active ingredient, of high fiber cereal diet responsible for cancer inhibition. A study investigated a) whether dietary fiber containing high IP6 shows an inhibition of artificially induced breast cancer, and b) if pure IP6 is more active as a cancer preventive agent, compared to that in the diet. Results showed that supplemental dietary fiber in the form of bran exhibited a modest, statistically nonsignificant inhibitory effect. In contrast, animals given IP6 in drink showed significant reduction in tumor numbers. Therefore, pure IP6 is definitively more effective than a high fiber diet in preventing experimental mammary tumors. Thus, for cancer prevention, prophylactic intake of IP6 may be not only more effective, but also more practical than gorging on large quantities of fiber.

14. **Prevention of colon cancer by components of dietary fiber**

Cancer of colon is one of the leading causes of cancer death in Western countries and is increasing rapidly in Japan. Studies have suggested that as the intake of fiber-rich food increases, colon cancer rates fall. Dietary fiber comprises a group of non-starch polysaccharides such as cellulose, hemicellulose, and pectin and non-carbohydrate substances such as phytic acid (inositol hexaphosphate) (IP6). Animal studies have consistently shown that dietary wheat bran reduced growth of colon tumors. Human studies have demonstrated that supplemental wheat bran in the diet decreased the formation of metabolites that have been shown to act as tumor promoters in the colon. Among the components of dietary fiber, especially wheat bran, inositol hexaphosphate (IP6) has been studied extensively for its chemopreventive properties against colon cancer in animals. Dietary IP6 reduced the incidence of colonic abnormal depression points, and changing pre-cancerous lesions in rats. Oral administration of IP6 was shown to inhibit colon cancer in rodents during the initiation and post-initiation stages. IP6 acts as an antioxidant, to reduce the rate of cell proliferation and to augment the immune system response by enhancing the activity of natural killer (NK) cells. This data provides evidence for potential chemopreventive properties of IP6 against colon cancer.

15. **Antiplatelet activity of inositol hexaphosphate (IP6)**

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3689-3693

Platelet adhesion to endothelial cells, their aggregation and subsequent release of platelet-derived mediators are key steps in the formation of blood clots and hardening of the arteries. The effect of inositol hexaphosphate (IP6) on platelet aggregation and adenosine triphosphate (ATP) (cells' energy storage) release were simultaneously measured in whole blood obtained from 10 healthy volunteers. The platelets were activated with adenosine diphosphate (ADP), collagen, or thrombin in the presence or absence of IP6. Inositol hexaphosphate (IP6) significantly inhibited platelet aggregation in a dose-response manner which were drug-induced. IP6 strongly and significantly reduced drug-induced ATP release for collagen and for thrombin. The results demonstrate that IP6 effectively inhibits human platelet aggregation in vitro, suggesting its potential in reducing the risk for cardiovascular disease.

16. **Inositol hexaphosphate (IP6) inhibits cancer and lowers lipids**

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3699-3702

IP6, a major dietary source of inositol phosphates, is a physiological antioxidant. Two studies examined the action of IP6 on dietary modulation of neoplasia (process leading to cancer) and hyperlipidemia (abnormally large amount of lipids in the blood) in rodents. One study examined the effect on the growth of tumors promoted in genetically identical rats transplanted with a viral cancer gene cell line. The results showed that increases in tumor incidence and growth rate seen following administration of a special diet (containing 5% saturated fatty acids and 1.2% magnesium oxide) were completely mitigated by supplementation of the same diet with purified potassium-magnesium phytate (containing 8.9% IP6 by weight). The other study examined the IP6 effect on blood lipid and mineral levels in animals fed a cholesterol-enriched or standard diet. Elevated levels of total blood cholesterol, triglycerides and zinc/copper ratio associated with administration of the cholesterol-enriched diet were significantly lowered by supplementation of this diet with monopotassium phytate. Addition of monopotassium phytate to the standard diet also reduced blood lipid levels but did not significantly affect the zinc/copper ratio. These studies support a role for IP6 as a potential therapeutic agent in the treatment of cancer and elevated blood lipids.

17. **The cancer problem**

Full source: *Anticancer Res* 99, Vol. 19, Iss. 5A, Pgs. 3787-3790

Cancer is mostly environmental in origin and therefore is theoretically preventable by control of environmental conditions. Neoplasia is the pathologic process that results in the formation and growth of a neoplasm, an abnormal tissue that grows by cellular proliferation more rapidly than normal and continues to grow after the stimuli that started the new growth cease. It occurs in steps, and generally has long latent periods. Neoplasia is a disease of the genes, with each tumor has its own alterations in gene patterns. Many carcinogens, mutagens (induce genetic mutations) and others, have been identified, and cancer prevention can now be promoted. The aim is to postpone symptoms of latent cancer to an older age. This has two

aspects: 1) the elimination of carcinogens from the environment and 2) active efforts to improve the lifestyle and develop effective chemopreventive agents. Understanding of prevention, understanding of molecular mechanisms of interactions between genes and environmental or dietary compounds for each cancer is essential.

18. Selenium deficiency and viral virulence

Full source: *Brit Med Bull* 99, Vol. 55, Iss. 3, Pgs. 528-533

Mice fed diets composed of low selenium ingredients from a Keshan disease area in China suffered more extensive heart damage when infected with a coxsackie B-4 virus than infected mice fed the same diet but supplemented with selenium. Selenium deficiency increased the virulence (capacity of a pathogen to overcome body defenses) of an already virulent strain of coxsackie virus and allowed conversion of a non-virulent strain to virulence. The conversion was accompanied by a change in the viral genome to more closely match that of the virulent virus. This is the first report of host nutrition influencing the genetic make-up of an invading pathogen. Nutritionists may need to consider this mechanism of increased viral virulence in order to gain a better understanding of diet/infection relationships.

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