

LE Magazine October 2001

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#### 1. SAME prevents vitamin E depletion in liver

S-adenosylmethionine (SAME) has been shown to reduce liver injury by preventing depletion of glutathione, one of the endogenous antioxidant systems that plays a critical role in defense against free radicals. In liver diseases, red blood cells may be decreased, and treatment with vitamin E reduces liver injury in rats. A study assessed whether SAME has any effect on liver red blood cells and vitamin C levels, in addition to restoring glutathione. In group 1, liver cirrhosis was artificially induced (injured). In group 2, SAME was added to similar group (10 mg/kg/day). The results showed that in injured rats, SAME decreased collagen content (3  $\mu\text{mol/g}$ ) and TBARS (stress marker), and corrected glutathione depletion. Vitamin E was significantly lower in the injured rats than in control groups (17 and 23  $\mu\text{mol/g}$  respectively). By contrast, vitamin E levels were similar (24  $\mu\text{mol/g}$ ) in injured rats receiving SAME and in controls. In injured rats, liver vitamin C was decreased in comparison with controls (5 and 8  $\mu\text{mol/g}$  respectively), levels which were not replenished by SAME (4.6  $\mu\text{mol/g}$ ). Thus, the results show that SAME not only decreases fibrosis (formation of fibrous tissue) and protects against the depletion of glutathione in the liver, but has a further antioxidant effect of preventing red blood cell depletion in chemically-injured rodents.

CLINICAL SCIENCE, 2000, Vol 99, Iss 4, pp 315-320

## 2. Bisphosphonates induce breast cancer cell death

Breast cancer frequently spreads to bone and is usually associated with loss of calcium. This loss of calcium, which is tumor-induced, increases bone reabsorption. Bisphosphonates are a class of drugs used successfully to inhibit bone resorption and dissolution in tumor bone disease. A study investigated the effects of bisphosphonates on breast cancer cells using four structurally different bisphosphonates: clodronate, pamidronate, ibandronate and zoledronate. They found that all four compounds induced a nonreversible inhibition of cancer growth in a time- and dose-dependent manner. Bisphosphonates induced apoptosis and cell necrosis in the cells. Thus, bisphosphonates inhibit breast cancer cell growth by inducing cell death in vitro.

JOURNAL OF BONE AND MINERAL RESEARCH, 2000, Vol 15, Iss 11, pp 2211-2221

### 3. Effect of nutritional status on viruses

The nutritional status of an individual is associated with both severity and susceptibility to infectious disease. The accepted rationale is that inadequate nutrition impairs the functioning of the immune system, thus resulting in increased susceptibility to infection. However, current studies suggest that not only can the nutritional status of the host affect the immune response, but it can also affect a virus. In mice, a benign strain of coxsackievirus B3 became virulent (competent to produce pathologic effects) and caused inflammation of the heart in selenium and vitamin E deficient mice. This change in pathogenicity was due to mutations in the viral genome, which changed a virus, which was not virulent into a virulent one. Once these mutations occurred, even mice with normal nutrition developed disease from the mutated virus. This suggests that the status of free radical stress of the individual can have a profound influence on the ability to invade tissues.

JOURNAL OF INFECTIOUS DISEASES, 2000, Vol 182, Suppl. 1, pp S93-S96

#### 4. Role of curcumin in eye cavity enlargement

A study documented, for the first time, the clinical efficacy of curcumin (the active constituent of rhizomes of *Curcuma longa* plant), in the treatment of those suffering from inflammatory eye cavity pseudotumors (enlargement). Curcumin was taken by eight individuals at a dose of 375 mg/3 times/day orally for a period of 6 to 22 months. They were followed up for a period of 2 years at three monthly intervals. Four out of the five that completed the study recovered completely. In one individual, the swelling regressed completely, but some limitation of movement persisted. No side effect was noted and there was no recurrence of enlargement. Thus, it is suggested that curcumin could be used as a safe and effective drug in the treatment of inflammatory eye enlargement.

PHYTOTHERAPY RESEARCH, 2000, Vol 14, Iss 6, pp 443-447

## 5. Melatonin restores full sexual activity in rats

Evidence exists that large doses of melatonin inhibit sexual performance in male rats. In contrast, small doses stimulate sexual activity of normal male rats. A study shows that administration of melatonin in small doses (10 to 100  $\mu\text{g}/\text{kg}$ ) induces the appearance of ejaculations in impotent male rats that were selected as showing no sexual approaches, mounts or ejaculations. The result suggests that melatonin may stimulate, in a dose-dependent manner, several copulatory parameters of male sexual behavior and may restore sexual activity in impotent animals by interacting with brain receptors, i.e. melatonin and serotonin receptors.

BRAIN RESEARCH, 2000, Vol 878, Iss 1-2, pp 98-104

## 6. Combination vitamin D3 therapy for liver cancer

A combination of vitamin D3 and a compound that blocks entry of calcium into cells like vanadium may offer a new approach to therapy and solve the problem of hypercalcemia (an excess of calcium in the blood) due to D3. Supplementation of vanadium, D3, or both vanadium and D3 were started in rats 4 weeks before liver cancer, and continued for 20 weeks. The results showed that supplementation of vanadium (0.5 ppm) in drinking water or vitamin D3 twice weekly for the entire period of the experiment significantly reduces the number and size of hyperplastic (abnormal increase in the number of normal cells, increasing organ size) nodules. The combination treatment offered an additive effect in reducing them to 37.5% from 83.3%. Vitamin D3 combination was also effective in elevating the level of liver microsomal cytochrome P-450 (enzymes involved in transfer of energy). There was a significant reduced level of glutathione in the vanadium plus D3 treated group, as compared to the cancer control group. Thus, vanadium may be useful in combination with vitamin D3 in the inhibition of liver cancer.

CHEMICO-BIOLOGICAL INTERACTIONS, 2000, Vol 128, Iss 1, pp 1-18

## 7. Melatonin vs. immunotoxicity of lead

The results of a study suggests that immunotoxicity induced by lead was significantly restored or prevented by melatonin (MLT). Melatonin was given to mice for 28 days, and lead at 35 mg/kg 2 hours after MLT. The following positive changes were recorded using lead + melatonin treatment: a) body weight and thymus gland significantly increased, b) spleen and liver weights that were increased by the treatment of lead alone, were restored to normal, c) cell response against red blood cell aggregation, and secondary IgG antibody response were significantly enhanced, d) response of T-cells (immune cells) to inhibit the growth of tumors and of B cells to lipopolysaccharides significantly increased, e) CD4(+) (immune) cells of the spleen significantly increased, f) slight enhancement of CD8(+) cells, g) T and B cells in the spleen significantly increased, and h) natural killer cell, phagocytic activity and the number of peripheral leukocytes (immune cells) were significantly enhanced in lead plus MLT-treated mice when compared with the treatment of lead alone.

INTERNATIONAL JOURNAL OF IMMUNOPHARMACOLOGY, 2000, Vol 22, Iss 10, pp 821-832

## 8. Free radical stress vulnerability in aging

Research indicates that vulnerability to oxidative stress (OSV) may increase in aging, suggesting that age-related neurodegenerative diseases such as Alzheimer's disease (AD) or vascular dementia (VAD) may be superimposed upon a vulnerable neuronal environment. Enhanced OSV may be the result of, (a) increases in membrane lipids, (b) decreases in glutathione and (c) CNS (central nervous sys.) distribution of OS-sensitive neuronal receptors. The combination of polyphenolics found in fruits (e.g. blueberry extract) with high antioxidant activity are among the most effective inhibitors of free radical stress. Experiments using dietary supplementation with fruit (strawberry) or vegetable (spinach) extracts have shown that such extracts are also effective in forestalling and reversing the deleterious effects of behavioral aging in rats. Thus, it appears that the beneficial effects of the polyphenolics found in fruits and vegetables in brain aging and behavior may be similar to those seen with respect to cancer and cardiovascular disease.

MECHANISMS OF AGEING AND DEVELOPMENT, 2000, Vol 116, Iss 2-3, pp 141-153

## 9. Anthocyanins enhance resistance to free radical formation

A study investigated the potential antioxidant properties of blueberries, using red blood cell (RBC) resistance to free radicals. Anthocyanins (flavonoids) significantly enhanced RBC resistance to free radicals which were induced by hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) production. Blood polyphenolic concentrations were highest after 1 hour, declining considerably after 6 hours and not detected after 24 hours. This protection shows a positive role following of consumption of dietary polyphenolics from blueberries, against free radical formation within red blood cells in vivo.

ALIMENTARY PHARMACOLOGY & THERAPEUTICS, 2000, Vol 14, Iss 10, pp 1303-1309

## 10. Free radicals and CNS nerve cells in Alzheimer's disease

The loss of nerve cells represents major abnormalities associated with dementia in Alzheimer's disease (AD). A study examined the role of free radicals as a contributing factor to both the cell death and degeneration of nerve cells in the central nervous system (CNS) in AD. Nerve cells were treated with hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) or desferrioxamine for 24 hours. The results showed that H<sub>2</sub>O<sub>2</sub> causes free-radical injury. Desferrioxamine causes hypoxia-type (reduction of oxygen supply to the tissue) injury without free radical generation. This suggests that free radicals can cause the degeneration of cells, which was associated with greater susceptibility to apoptosis (cell death). This was due to the activation of certain genes that promote apoptosis, neurite retraction (a disconnection between excitable nerve cell outgrowths, i.e. dendrites/axons, at the synapse), and impaired transport of mitochondria to the cell processes where they are likely required for synaptic function (sending/receiving nerve impulses). Desferrioxamine treatment resulted in loss of nerve cells associated with impaired mitochondrial function, proliferation (sprouting) of neurites, and reduced activity of GAP-43 (plays a role in path-finding during neurite outgrowth). Hypoxia-type injury causes nerve loss with proliferation of neurites, impaired mitochondrial function, and reduced activity of molecules required to form and maintain synaptic connections. Therefore, since similar abnormalities occur in Alzheimer's disease, both free radical stress and injury due to loss of oxygen can contribute to Alzheimer's nerve cell degeneration.

CANCER RESEARCH, 2000, Vol 60, Iss 20, pp 5617-5620

## 11. Calorie restriction decreases proinflammatory proteins

Calorie restriction or fish oil (enriched in n-3 fatty acids) supplementation weaken kidney disease and Sjogren's syndrome lesions in mice. A study examined the effect of calorie restriction and fish oil supplementation on the activity of key inflammatory proteins [gamma interferon (INF-gamma), interleukin-10 (IL-10) and IL-12] and immunoglobulin (Ig) receptor. Mice were fed either unlimited food (UL) or calorie restricted (CR) (40% less calories than UL) diets supplemented with 5% corn oil or 5% fish oil for up to 9 months of age. Results revealed a significant increase with age in UL fed mice, in the activity of IFN-gamma, IL-10, IL-12 mRNA and PIgR mRNA. However, CR fed mice maintained their levels to near those seen in young animals regardless of the dietary fat. Calorie restriction therefore significantly inhibits the elevated levels of the protein, immunoglobulin-A in aged mice. The results indicate that calorie restriction can lessen autoimmune disease in mice.

JOURNAL OF CLINICAL IMMUNOLOGY, 2000, Vol 20, Iss 5, pp 354-361

## 12. Vitamin E, membrane fluidity and blood pressure

Vitamin E treatment was found to lower blood pressure, and increase red blood cell membrane fluidity in hypertensive and normal rats. The rats were given vitamin E, 3 days/week for 3 weeks. The degree of resistance of the membranes to splitting in vitamin E treated hypertensive and normal rats were lower than were those of the controls. The vitamin E treated hypertensive and normal rats showed significantly lower blood pressure than the control group.

LIFE SCIENCES, 2000, Vol 67, Iss 15, pp 1881-1889

### 13. Melatonin: potent scavenger of free radicals

The endogenous antioxidative defense system reduces the toxicity to molecules from oxygen and nitrogen-based free radicals. Melatonin is an efficient direct and indirect antioxidant. It detoxifies the highly reactive hydroxyl free radical and neutralizes other toxic radicals, including singlet oxygen, hydrogen peroxide, nitric oxide and peroxyxynitrite anion, and stimulates several antioxidative enzymes.

NEWS IN PHYSIOLOGICAL SCIENCES, 2000, Vol 15, pp 246-250

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