LE Magazine April 1997

REPORT

New Studies on Melatonin

On average, eleven new studies on melatonin appear in the scientific literature every week. The Life Extension Foundation reviews every single one of these studies in order to recommend safe and effective melatonin dosing for the prevention of disease. The most important new studies relating to melatonin's anti-aging effects are discussed in this article.

PROTECTING AGAINST BRAIN AGING

melatonin has been shown to protect brain cells against free radical attack and age-related degenerative changes. Brain cells have extraordinarily high energy needs. The byproduct of the conversion of this energy is free radicals. The brain, which has a high fat content, is especially vulnerable to damaging free radicals (lipid peroxidation). Since brain cells have little to no ability to rejuvenate, it is critical to protect them. For this reason, the blood-brain barrier limits what can reach the brain. This is a problem when one wants to deliver protective molecules such as antioxidants. Melatonin is an antioxidant that can "break through" the barrier and reach the brain. It is a "lipophilic" agent that can get into cell membranes to provide direct antioxidant protection to the delicate structures within brain cells.

In a study in *Free Radical Biology and Medicine (21:2, 1996)*, melatonin protected dopamine-producing neurons against the damaging effects of catecholamine autoxidation. This finding provides further evidence that melatonin supplementation over age 40 could help to protect against Parkinson's Disease.

In a study in the Journal of Pineal Research (May, 1996), kainate-induced oxidative stress was measured in brain cell membrane receptors. Kainate-induced neurotoxicity is another mechanism of free radical damage in the brain. Melatonin was able to reduce the number of iron-induced oxygen radicals in rats injected with kainate in vivo. The scientists found that 73% of the control rats died within five days while the melatonin-supplemented group had a significant reduced mortality rate. Melatonin protected these rats from acute free radical induced death while the control group not receiving melatonin died within five days!

Another study, published in the Journal of Pineal Research (May, 1996) on kainate induced DNA damage, confirms the protective effect of melatonin against this very toxic substance. Autopsy microscopy of the hippocampal area of the brain revealed that melatonin reduced the amount of cellular DNA damage.

LOWERING BODY TEMPERATURE AND AGING

In two studies, mice given supplemental melatonin lived longer than mice not receiving melatonin. In a study in the Journal of Pineal Research (May, 1996), melatonin lowered nighttime body temperature levels in humans. The higher the dose of melatonin, the greater the reduction in core body temperature.

In longevity studies by Liu and Walford in cold-blooded annual fish, the lowering of body temperature doubled their lifespan. While it proved difficult to reduce body temperature chronically in warm-blooded animals, Dr. Roy Walford of UCLA Medical Center has long believed that lowering body temperature safely in humans might extend lifespan. Supplemental melatonin may help do just that.

One of melatonin's mechanisms in promoting sleep is to lower body temperature in the early hours of the morning, which enables people to enter into deep "hibernation-like" sleep that is revitalizing and rejuvenating. Melatonin is the first substance that has been shown to safely and effectively lower core body temperature in humans.

The scientists found that 5 mg of melatonin produced the most significant and sustained body temperature drop in humans. The title of the *Pineal Research Journal* paper is: "The hypothermic effect of melatonin on core body temperature: Is more better?"

ANTI-CANCER EFFECTS

There are several hundred published papers documenting melatonin's effectiveness as an adjuvant cancer therapy. One mechanism of melatonin's action is the boosting of immune system components that attack cancer cells. Melatonin has also been shown to promote cancer cell differentiation into normal cells, and to inhibit cancer cell proliferation.

In a study in the Journal of Biological Regulators and Homeostatic Agents (Oct-Dec 1995), 40 mg a night of melatonin was given in combination with low doses of interleukin-2 to 11 AIDS patients whose T-helper cell count had fallen below 200. After only three weeks of therapy, T- helper cells had risen more than 30% in 36% of the patients. In addition, the treatment produced a significant increase in the mean number of eosinophils, T lymphocytes, and natural killer cells. Finally, the important T-helper:T-suppressor ratio significantly increased during this study. The scientists concluded that the addition of melatonin could be an effective immune enhancing therapy for AIDS patients who do not generally respond to IL-2 alone.

The study provides additional evidence that melatonin and IL-2 can work synergistically to enhance immunity which is also crucial in cancer patients. What make this study important for healthy people is that aging causes a progressive decline in immune function, and melatonin appears to significantly restore immune function.

ANOTHER IMMUNE PROTECTING MECHANISM

One mechanism by which immune function is suppressed in both AIDS and cancer patients is the excessive release of the cortisol. It has been hypothesized (Medical Hypotheses, July 1996) that melatonin may be able to block excess cortisol metabolism, thereby protecting immune cells from the deleterious effects of cortisol. Aging causes elevated serum cortisol levels in most people. Cortisol has a destructive effect on cells throughout the body. This leads some scientists to call cortisol one of the "death hormones". The "death hormone" theory of aging states that humans secrete certain deleterious hormones that directly cause cells to age and die. If melatonin can block excess cortisol metabolism, then this would represent a potent anti-aging effect.

Studies have documented the effects of melatonin and zinc in regenerating the thymus, and enhancing hormonal output. A new study in the *Journal of Pharmacological Experimental Therapy (June 1996)* shows the synergistic relationship that zinc and melatonin have in restoring lost thymic hormone output.

Melatonin Prevention Formula contains 20 mg of OptiZinc to enhance the ability of melatonin to restore thymic hormone output. Most Foundation members already take 30-to-60 mg of zinc. The new formula provides a highly absorbable form of zinc with 5 mg of melatonin. The maximum safe intake of zinc on a chronic basis is 90-to-120 mg. a day.

VITAMIN D3: THE ANTI-CANCER VITAMIN

The most widely studied vitamin for the prevention and treatment of cancer is vitamin D3. Numerous studies document the ability of vitamin D3 to induce cancer cells to differentiate into normal cells and to interfere with cancer cell division. Vitamin D3 appears to be especially protective against breast and prostate cancer, and has been shown to be an effective adjuvant therapy against leukemia, lymphoma and brain cancers.

Unlike most vitamins, vitamin D3 has a narrow therapeutic range. Too much vitamin D3 can be toxic, but not enough predisposes people to cancers (such as breast and prostate) that may not be prevented by antioxidants.

Vitamin D3 functions more like a hormone than a vitamin. It regulates calcium metabolism throughout the body and induces normal cellular differentiation.

A moderate amount (300 iu) of vitamin D3 is contained in the daily dose of the Life Extension Mix(tm). The Mineral Formula for Women contains 100 i.u. of vitamin D3 in each capsule. Women are encouraged to take 6-to-8 capsules a day to protect against osteoporosis.

Based upon new research indicating the cancer prevention role of vitamin D3, 400 iu of pharmaceutical-grade (ROCHE) vitamin D3 to enhance the effectiveness of melatonin in preventing breast and other cancers.

The ideal daily intake of vitamin D3 may be between 700 iu and 1,500 iu for cancer prevention, depending on individual variability. A standard blood chemistry test to measure calcium levels can determine if too much vitamin D3 is being consumed.

Cancer patients should consider taking 2,000 to 3,000 iu of vitamin D3 a day, with monthly blood tests to guard against toxicity. Those with pre-existing kidney disease should not take high doses of vitamin D3.

CAUTION:
Anyone going on a high-dose nutrient/drug supplement program aimed at the prevention and/or treatment of any disease or condition should only do so under the care of a physician who uses regular blood testing to monitor progress and potential toxicity.

CLA: THE ANTI-CANCER FAT

The last ingredient in Melatonin Prevention Formula is Conjugated Linoleic Acid (CLA). CLA is a component of beef and dairy products that has been shown to protect against cancer, especially breast cancer.

In a study in Anticancer Research (December 6, 1992), human breast cancer cells were inhibited 54-100% following 8-to-12 days of treatment with varying doses of CLA. The higher the dose of CLA, the greater the extent of cell growth inhibition.

In a cell culture study in Cancer Letters (63:2, 1992), CLA reduced human breast, colorectal and melanoma cell proliferation by 18-100% compared to control cultures. CLA inhibited the incorporation within cells of growth factors such as thymidine that are required for cancer cells to grow. Soy isoflavones inhibit cancer cell growth via a similar mechanism.

In a study in Cancer (74:9, 1994), CLA protected against mammary cancer in rats, even when exposure to CLA was limited to only a brief point in the animal's life. The scientists concluded that CLA is unique because its anticancer effect occurs at concentrations compatible with reasonable human consumption levels.

In a study in Cancer Research (54:7 1994), scientists at the Roswell Park Cancer Institute found that the addition of two anticarcinogens to foods reduced the risk of human breast and other forms of cancer. The first anticarcinogen was selenium from garlic; the second was CLA.

CLA is an antioxidant, but its mechanism of action extends beyond its ability to inhibit free radicals.

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