

## Melatonin:

Melatonin is a substance produced by the pineal gland in the brain. This gland is about the size of a kernel of corn. It produces melatonin in response to low light or dark environments. Melatonin levels are very low during the day and increase when a person is in a dark place getting ready for sleep. Melatonin also declines with age. By the time a person reaches fifty the melatonin levels are less than half of the levels produced in childhood.

Melatonin appears to help with jet lag and changes in sleep schedule. Melatonin helps reset the body's internal biological clock. This is important to improving sleep quality and total time asleep when changing your sleep schedule. Melatonin, however, is not a sleeping agent. It only tells your brain that it is dark outside.

The internal body clock regulates the body hormonal and temperature rhythms. Without melatonin, the internal body clock can change approximately one half hour per day. Thus a hour change in sleep schedule will take approximately two days. This ability to change decreases with age. If not given any time cues, the internal clock generally runs about 24.5 hours. This is why it is easier to travel west than to travel east.

As the hormone which helps tell the brain that it is dark, melatonin can help regulate the time to go to sleep than the traditional sleeping pills. There is some speculation that melatonin may help the sleep quality of older individuals. However this has not been uniformly demonstrated in studies.

Melatonin has very few side effects. People have taken as much as 75 milligrams of melatonin in carefully monitored studies with no signs of toxicity. The only consistent side effect of high doses has been drowsiness occasional headache, stomach aches, agitation excessive dreaming and a slower reaction time. Additionally, the Food and Drug Administration reports that in the more than two years that melatonin has been available for sale over-the-counter, no alarming negative side effects have been reported. Some people who have experienced one or more of these reactions have found that taking a lower dose or switching to a different brand, or taking a brand that does not contain vitamin B6, seems to help. People who continue to experience negative side effects should stop taking melatonin.

There is also anecdotal evidence that melatonin worsens depression in some people. For this reason, we advise that people who are depressed consult their physicians before taking melatonin.

Animal studies suggest that melatonin can cause temporary narrowing of the blood vessels supplying the heart and brain. Therefore, if you have problems with blood pressure, heart disease or strokes, you should not take melatonin

It is always best to err on the side of caution. **We recommend that the following people not take melatonin at the present time, or take it only with the advice and close supervision of a physician:**

- People taking prescription steroid drugs
- Women wanting to conceive
- Pregnant women and nursing mothers
- People with severe mental illness
- People with heart disease, strokes or high blood pressure
- People with severe allergies
- People with autoimmune diseases
- People with immune-system cancers such as leukemia and lymphoma
- Normal children of all ages

Although melatonin has been tested on humans in several studies, it has not been administered in the large-scale, carefully controlled studies necessary to determine its ultimate safety. People who choose to take melatonin at the present time are facing some unknown risks.

The dose of melatonin for sleep onset may vary from individual to individual. Many people start with a 0.5 to 3.0 milligrams dose and either increase or decrease the dose as needed. (The dose is too high if you feel groggy the next morning; it may be too low if you do not experience a deep, restful sleep. Ten milligrams is the highest dose currently being recommended. Doses higher than this may cause elevated levels of melatonin the next day.)

You should take the melatonin approximately twenty minutes prior to going to bed. Your pineal gland produces melatonin only at night, and the goal is to supplement your body's natural processes. Therefore, if you are trying to sleep during the daytime you should make sure the bedroom is dark so that you can increase the melatonin secretion.

Many companies are now marketing melatonin. Some of the products are labeled "natural" melatonin and are reputed to contain actual extracts of the pineal gland. You should avoid these products. If the pills contain actual animal tissue, they may be contaminated with viruses or proteins which may be dangerous. You should buy synthetic melatonin. The synthetic melatonin is made from pharmaceutical grade ingredients and is molecularly identical to the melatonin you produce in your own body.

Synthetic melatonin is now available in three different preparations---regular, time-release, or sublingual. Regular melatonin tablets produce an initial spike of the hormone in your bloodstream, much higher than normally present in your body. Time-release tablets allow melatonin to enter your bloodstream more gradually, and therefore extend the time of release of melatonin in your blood stream. This way you can take a low dose and still have melatonin in your bloodstream throughout the night. Sublingual melatonin enters your bloodstream the most rapidly because some of it is absorbed by the lining of your mouth, entering your bloodstream directly. Sublingual tablets cause a quick rise in the level of melatonin but then will drop off and may not extend your sleep. If your goal is to replicate the body's actions, then a small dose (approximately 1 mg), time-release tablet may be the best choice.

We recommend that you buy a preparation that does not contain additional ingredients (other than the inert binder/filler.) Studies have not been done on these various combinations, so little is known about their safety or efficacy. Furthermore, more negative side effects are associated with some of these products - especially vitamin B-6.

There are dozens of different companies now offering melatonin and they obtain the raw material from one of a half-dozen suppliers. This raw material varies in purity. The following companies have undergone independent testing for purity of the melatonin and have received high ratings. (We have no financial interests in these companies.)

Allergy Research 1-800-545-9960 (Outside U.S.--- 510-639-4572)

KAL -- Available in local health food stores

Life Extension -- 1-800-841-5433 (Outside U.S.--- 305-966-4886)

Natrol -- Available in local health food stores

Wholesale Nutrition -- 1-800-325-2664 (Outside U.S.--- 408-867-6368)

Locally several stores have stocked melatonin. These include and are not limited to General Nutrition Center, Well Spring Grocery, Weaver Street Market and Eckards Pharmacy. We are sure more stores will have melatonin on their shelves.

Storage of your melatonin may be important especially if you buy in large quantities and allow the melatonin to stay on the shelf for several weeks. Melatonin may be heat sensitive and thus some pharmaceutical companies recommend that you store the melatonin in the refrigerator.

**Hopefully you will find this information helpful. If you have questions regarding melatonin and your own health please contact your physician**

## 2. What will it do for me?

Melatonin serves two fundamental roles in your body---hormonal regulation and antioxidant protection. In its hormonal role, melatonin influences reproduction, boosts the immune system, regulates the body clock, enhances sleep, influences the cardiovascular system, and may help protect against cancer. (In test tube studies, melatonin has slowed the growth of seven different kinds of human cancer cells, including breast and prostate cancer cells.)

In its antioxidant role, melatonin has been shown to be an extremely potent and wide-ranging antioxidant, protecting every part of the cell and every cell in the body, including vital brain cells. Antioxidants are vital to your health because they rid the body of dangerously reactive molecules called "free radicals." Over 100 diseases have now been linked with free radical damage, including cataracts, macular degeneration, Alzheimer's disease, Parkinsonism, arthritis, cancer, and the aging process itself.

Because melatonin plays so many diverse roles in your body, taking supplemental melatonin has been shown to enhance your health in a surprising number of ways. For example, clinical studies have shown that melatonin is an effective remedy for insomnia, jet lag, and shiftwork maladaptation. It also shows promise as a treatment for a number of other diseases and conditions, including hypertension, high cholesterol, AIDS, various kinds of cancer, autism, epilepsy, migraine, arthritis, fetal alcohol syndrome, and Alzheimer's disease. Perhaps the most startling finding is that taking small amounts of melatonin on a nightly basis, starting in middle age, may extend your healthy, productive years.

## 3. Is it safe?

Melatonin is one of the least toxic substances known. People have taken as much as 6 grams of the substance in carefully monitored studies with no signs of toxicity. The only consistent side effect of high doses has been drowsiness and a slower reaction time. In the most extensive clinical trial to date, a very high dose of melatonin---75 milligrams---has been given to 1400 women for up to four years with no significant ill effects. Furthermore, the Food and Drug Administration reports that in the more than two years that melatonin has been available for sale over-the-counter, no alarming negative side effects have been reported.

However, although melatonin has been tested on humans in hundreds of studies, it has not been administered in the large-scale, carefully controlled studies necessary to determine its ultimate safety. People who choose to take melatonin at the present time are facing some unknown risks.

## 4. How much should I take?

Hundreds of thousands of people have decided not to wait for further study results and have begun to take melatonin. One of their most commonly asked questions is: "How much should I take?"

There is no simple answer. Melatonin researchers themselves have yet to determine the optimum doses for various uses. Furthermore, the same dose of melatonin can result in widely differing blood levels in different individuals. (In one study, five healthy volunteers took the same 2 milligram dose of melatonin. There was a 35-fold difference in the amount of melatonin that entered the bloodstream.)

For purposes of sleep, many people start with a 1 milligram dose and either increase or decrease the dose as needed. (The dose is too high if you feel groggy the next morning; it may be too low if you do not experience a deep, restful sleep. Ten milligrams is the highest dose currently being recommended. Doses higher than this may cause elevated levels of melatonin the next day.)

For a suggested range of doses for jet lag, anti-aging, antioxidant protection, immune stimulation, AIDS, cancer therapy, and PMS, see pages 210-211 of Melatonin-Your Body's Natural Wonder Drug.

5 What time of day should I take melatonin?

Unless your physician advises otherwise, always take melatonin at night. Your pineal gland produces melatonin only at night, and the goal is to supplement your body's natural processes, not subvert them. Taking melatonin in the daytime can have negative effects, including resetting your body clock-giving you unintentional "jet lag"- or making you drowsy and increasing your risk of accidental injury.

If you have difficulty falling asleep, take melatonin about an hour before bedtime. If you have difficulty staying asleep, take it when you retire.

6. Which kind should I buy?

Many companies are now marketing melatonin. Some of the products are labeled "natural" melatonin and are reputed to contain actual extracts of the pineal gland. Stay away from these products. If they contain actual animal tissue, they may be contaminated with viruses or proteins that could evoke an antibody response. Buy synthetic melatonin. Synthetic melatonin is made from pharmaceutical grade ingredients and is molecularly identical to the melatonin you produce in your own body.

Synthetic melatonin is now available in three different preparations---regular, time-release, or sublingual. Regular melatonin tablets produce an initial spike of the hormone in your bloodstream, much higher than normally present in your body. This is not ideal. Time-release tablets allow melatonin to enter your bloodstream more gradually, mimicking your body's natural mode of production. This way you can take a low dose and still have melatonin in your bloodstream throughout the night. Sublingual melatonin enters your bloodstream the most rapidly because some of it is absorbed by the mucus membranes, entering your bloodstream directly. Sublingual preparations also allow a higher percentage of the melatonin to be utilized because less of it is metabolized in the liver. However, sublingual tablets have the same disadvantage as regular tablets in that they generate high initial blood levels of melatonin, quite unlike the body's natural circadian production. If your goal is to replicate the body's actions, then a small dose (approximately 1 mg), time-release tablet may be the best choice.

We recommend that you buy a preparation that does not contain additional ingredients (other than the inert filler.) Studies have not been done on these various combinations, so little is known about their safety or efficacy. Furthermore, more negative side effects seem to be associated with these products -- especially those that contain vitamin B-6.

There are dozens of different companies now offering melatonin and they obtain the raw material from one of a half-dozen suppliers. This raw material varies in purity. We recommend the following companies because their melatonin has undergone an independent test for purity and received high ratings. (Note: We are not financially linked with these or any other melatonin suppliers.) More names will be added to the list as we receive updated information.  
Allergy Research 1-800-545-9960 (Outside U.S.--- 510-639-4572)

KAL -- Available in local health food stores

Life Extension -- 1-800-841-5433 (Outside U.S.--- 305-966-4886)

Natrol -- Available in local health food stores

Wholesale Nutrition -- 1-800-325-2664 (Outside U.S.--- 408-867-6368)

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#### 7. What are possible negative side effects?

There is anecdotal evidence that a small percentage of the people taking over-the-counter melatonin have experienced an atypical reaction, becoming agitated rather than sleepy or having so many dreams that their sleep does not feel restful. Others have complained of headaches or stomach aches. These negative reactions have not been observed in clinical trials. Some people who have experienced one or more of these reactions have found that taking a much smaller dose has eliminated the problem. Others have found that switching to a different brand, or taking a brand that does not contain vitamin B6, seems to help. People who continue to experience negative side effects should stop taking melatonin.

There is also anecdotal evidence that melatonin worsens depression in some people. For this reason, we advise that people who are depressed consult their physicians before taking melatonin. It should also be noted that many people experience a profound relief from depression while taking melatonin. Melatonin's effects on mood is a sadly neglected area of research.

#### 8. Are there any people who should not take melatonin?

It is always best to err on the side of caution. We recommend that the following people not take melatonin at the present time, or take it only with the advice and close supervision of a physician:

- People taking prescription steroid drugs
- Women wanting to conceive
- Pregnant women and nursing mothers
- People with severe mental illness
- People with severe allergies
- People with autoimmune diseases
- People with immune-system cancers such as leukemia and lymphoma
- Normal children of all ages

In our book, we explain the reasons for these contraindications. In our book, we explain the reasons for these contraindications.

#### 9. How does melatonin affect sexuality?

Currently, there is a great deal of misinformation about melatonin's effects on human sexuality. What does the research show? In animals, seasonal changes in light levels cause the pineal gland to produce increased amounts of melatonin. The surge of melatonin will either inhibit or stimulate the reproductive organs, depending on the species.

The human reproductive system does not react so predictably or strongly to the hormone. Very high doses of melatonin (75 milligrams) in a time-release formulation, when coupled with progesterone, will inhibit ovulation in most women. (A contraceptive based on this formulation is now beginning Phase III clinical trials.) Smaller doses of melatonin, as little as 10 milligrams, may inhibit ovulation in a small percentage of women. There is also a growing body of anecdotal evidence that melatonin may reduce excessive or prolonged menstrual flow and reduce the symptoms of PMS.

Men have not been given high doses of melatonin for prolonged periods of time. However, it is known that 2 milligrams of melatonin taken for several months at a time has no effect on testosterone levels.

Will melatonin enhance your sex life, a claim currently being made in some melatonin books? There is no evidence this is so. However, a 1995 rodent study produced an intriguing finding. Male rats that were given small doses of melatonin on a nightly basis did not experience the expected age-related decline in testosterone levels. As a result, at old age, the melatonin-treated

rats had 3-4 times the testosterone levels as the control rats.

#### 10. Will melatonin really extend my lifespan?

There are no human studies to support this contention. However, melatonin has caused a significant (20%) increase in lifespan in both rats and mice. If melatonin does indeed allow you to live longer, it may be due to its proven ability to:

- Reduce free radical damage
- Stimulate an aging immune system
- Protect the cardiovascular system
- Preserve a youthful circadian rhythm
- Stimulate the production of growth hormone

Each of these five properties is explored in detail in our book.

From: jor@teleport.com (Jo Robinson)  
Newsgroups: sci.med.pharmacy  
Subject: Re: Melatonin and epilepsy  
Date: 18 Nov 1995 19:31:06 GMT

teresa blackwell (paul951@ix.netcom.com) wrote:  
: I am a mini mall eplieptic who takes tegretol (1000 mg)  
: and mysoline (250mg) a day. Will using melatonin have any  
: adverse effect on me?

Melatonin has been shown to have anti-convulsant properties,  
both in animals and humans.

IN an early human study, melatonin was injected into a number  
of volunteers with epilepsy. According to the researcher, "Melatonin  
administration was followed by a progressive decrease in the amplitude  
administration was followed by a  
progressive decrease in the amplitude  
of the electrical activity of the temporal lobe with a general tendency to the  
synchronization of the amygdala and the cortex." ONe patient was kept  
on melatonin for 2 days and remained seizure free, despite the withdrawal  
of his customary medications. [Life Sciences 1971; 10:841-50]

A more recent finding is that melatonin lowers the excitability of  
individual neurons. [Melatonin: Biosynthesis, Physiological Effects,  
and Clinical Applications Baton Rouge: CRC Press 1993]

Large-scale clinical trials have not been conducted using melatonin  
as a therapy for epilepsy, so the researchers' knowledge is limited. However,  
I know of no adverse effects that would come from taking it.

We discuss the relationship between melatonin and epilepsy  
in more detail in our recently published book, Melatonin: Your  
Body's Natural Wonder Drug. Russel J. Reiter and Jo RObinson  
Bantam 1995. (Pages 221-222.)