

**Products**

**What is the proper dose of melatonin?**

Based on published reports indicating significant disease prevention potential, melatonin has become a popular dietary supplement in the United States. There is a debate, however, as to what the optimal nightly dose of melatonin should be.

A recent study tested ten milligrams of melatonin for 28 consecutive nights on human volunteers. At this high dose, there was no evidence of toxicity and those receiving the melatonin (10 mg) had a better sleep score compared to the placebo group.(1)

Some experts, however, advocate that low-dose melatonin is better than higher doses. These scientists point to another study on human subjects where only 300 micrograms of melatonin induced better sleep than 3000 micrograms (3 mg) over a seven day period.(2)

A review of all the published literature reveals that a wide range of melatonin doses have been used to produce better sleep patterns in human subjects.(3-31)

The Life Extension Foundation introduced melatonin to its members in 1992. The dosage unit of the first melatonin supplement offered was 3 milligrams (mg). Over the years, The Foundation has introduced new melatonin supplements starting in dosage units of 500 micrograms and going up to 10 milligrams.

In the January 1996 issue of Life Extension magazine, an article was published suggesting that lower doses of melatonin might enable some people to sleep better. This article was based on anecdotal reports from some members who stated they had better sleep patterns when taking 500 microgram melatonin rather than higher doses.

To ascertain what dosage units Foundation members find most effective, we did a computer survey of melatonin purchases over the last 12 months. The chart below shows the percentage of overall melatonin sales for the least to most popular doses of melatonin chosen.

Percentage of Overall:	
Melatonin Sales	Melatonin Dose
500 mcg (micrograms)	2.24 %
10 mg (milligrams)	6.99 %
1 mg	8.19 %
5 mg (Natural Sleep)	14.07 %
3 mg (sub-lingual)	14.68 %
3 mg (time-release)	20.06 %
3 mg	33.76 %

As can be seen above, the majority of Foundation members prefer the 3 mg doses. Even

**Melatonin's multi-modal effects**

Melatonin may help prevent a number of age-related degenerative diseases. What follows are titles from just a few of the many published articles indicating the importance of maintaining youthful levels of melatonin.

A significant correlation between melatonin deficiency and endometrial cancer. *Gynecol Obstet Invest* 1998; 45(1):62-5.

Melatonin and regulation of the cardiovascular system. *Therapie* 1998 Sep-Oct;53(5):459-65.

Effect of melatonin on sleep quality of COPD intensive care patients: a pilot study. *Chronobiol Int* 2000 Jan;17(1):71-6.

Pharmacology and physiology of melatonin in the reduction of oxidative stress in vivo. *Biol Signals Recept* 2000 May-Aug; 9(3-4):160-71.

Is carbonyl detoxification an important anti-aging process during sleep? *Med Hypotheses* 2000 Apr;54(4):519-22.

Differential growth inhibitory effect of melatonin on two endometrial cancer cell lines. *J Pineal Res* 2000 28(4):227-33.

though most people are buying the 3 mg size, some are taking two of these capsules at bedtime, meaning they are consuming a total of 6 mg of melatonin nightly.

Based on studies indicating that melatonin may provide anti-aging effects throughout the body, it is easy to understand why members would want higher amounts of melatonin. One recent report discusses the role of melatonin in reversing partially degraded body proteins that lead to lipofuscin (age-pigments), cataract and cross-linked collagen. The scientist who wrote this article stated that the night-time rise in melatonin is one way the body "cleans" itself of partially glycated proteins.(32) If this hypothesis is correct, it provides a new mechanism to help explain how melatonin protects against such a wide range of age-related diseases.

For those who are not sleeping well, despite taking higher doses of melatonin, it is important to emphasize that there is a logical basis for some people using lower doses to induce better sleep.

The age-related decline in melatonin production

As people age, their sleep quality often undergoes significant deterioration, commonly characterized by frequent and longer-lasting nighttime awakenings. In many older people, sleep disturbance is correlated with a decline in melatonin secretion. A number of published studies also show that decreased melatonin production is associated with the onset of a host of degenerative diseases.(53-57)

In older people, peak nighttime melatonin levels are only 30 to 40 (picograms per milliliter of blood),(58) whereas younger people often secrete 100 to 200 (picograms per milliliter of blood) at night.(59) This age-related decline in melatonin secretion has been demonstrated in all but one(60) of more than 20 studies that have examined this issue.

The vast majority of melatonin is produced in the pineal gland. During normal aging, calcification of the pineal tissue is thought to cause the decline in melatonin synthesis.

A number of studies show that melatonin deficiency may be an underlying cause of insomnia in older people. When melatonin is administered to humans in clinical trials, it induces sleep sooner and produces better sleep patterns compared to placebo.(61-64)

Low-dose melatonin for sleep

In response to several studies showing that doses as low as 300 micrograms of melatonin can induce an enhanced state of drowsiness and provide a better quality of sleep, The Life Extension Buyers Club is offering members the option of using very low-dose melatonin supplements. For those who have tried higher dose melatonin supplements and not found effective relief from insomnia, these lower dose supplements may prove effective.

Here are the three new low-dose melatonin supplements being offered

	Retail	Member Price
Melatonin 300 microgram (mcg)/ 100 capsules	\$5.75	<b>\$4.31</b>
Melatonin 300 mcg time-release/ 100 capsules	\$6.25	<b>\$4.69</b>
Melatonin 750 mcg time-release/ 60 capsules	\$5.75	<b>\$4.31</b>

Unlike Canada, Europe and Japan, where melatonin is regulated as a drug, citizens of the United States can buy pharmaceutical-grade melatonin at extraordinarily low prices.

When it comes to ascertaining the ideal dose of melatonin, there appears to be a wide range of individual variability. Most people use 3 mg of melatonin at night to induce better sleep and saturate their body with high levels of melatonin. There will be some people, on the other hand, who may find they sleep better by taking only 1/10 this amount, i.e. 300 mcg of melatonin.

Mainstream scientists often raise concern that melatonin sold in health food stores may not meet pharmaceutical standards of purity. That is why the Life Extension Buyers Club restricts its purchases of melatonin to European sources that produce only 99.99% or better purity.

Melatonin as biological response modifier in cancer patients  
Anticancer Res 1998 Mar-Apr;18 (2B):1329-32.

Melatonin deficiency: Its role in oncogenesis and age-related pathology. Journal of Orthomolecular Medicine (Canada) 1990, 5/1 (22-24).

Cataractogenesis and lipid peroxidation in newborn rats treated with buthionine sulfoximine: preventive actions of melatonin. J Pineal Res 1997 Apr;22(3):117-23.

Melatonin improves sleep quality of patients with chronic schizophrenia. J Clin Psychiatry 2000 May;61 (5):373-7.

Effect of melatonin on proliferative activity and apoptosis in colon mucosa and colon tumors induced by 1,2-dimethylhydrazine in rats. Exp Toxicol Pathol 2000;52(1):71-6.

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