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Report

## Beyond Sleep: 7 Ways Melatonin Attacks Aging Factors

By Claudia Kelley, PHD, RD, CDE



Melatonin is known for helping some people achieve a better night's sleep, which is how it earned its nickname as "the sleep hormone."

While melatonin is involved in regulating our internal body clock, that's just the beginning of its health-promoting benefits. Based on extensive research, scientists have discovered that this hormone has beneficial effects on everything from heart disease and diabetes, to bone health and obesity. And best of all, emerging science now suggests that it may protect our genetic material and guard against age related disease and decline.<sup>1</sup>

Preclinical studies found that melatonin increased the life span of animals by up to **20%**—prolonging their youthful character in the process.<sup>2-4</sup> Scientific evidence now suggests that melatonin plays a crucial role in a variety of metabolic functions,<sup>5</sup> including antioxidant and neuroprotection,<sup>6,7</sup> anti-inflammatory defense,<sup>8</sup> and immune system support.<sup>9</sup>

Because melatonin production reduces with age,<sup>10-14</sup> experts believe that its decline contributes to both the aging process and a generalized deterioration of health.<sup>5,15-17</sup> Years ago, scientists could only speculate at the underlying mechanisms behind melatonin's anti-aging properties. A growing body of evidence reveals how melatonin is able to play such a major role in the combating aging process.<sup>18-20</sup>

### #1: Antioxidant Defense—Combat Free Radical Damage While You Sleep

Since its discovery over 50 years ago, melatonin has demonstrated itself as a functionally diverse molecule, with its antioxidant properties being amongst its most well-studied attributes.<sup>26,27</sup> Since then, a vast amount of experimental research has revealed its vital role in the body's defense against numerous cell-damaging free radicals—and for good reason.<sup>27-30</sup> Melatonin has been found to possess **200%** more antioxidant power than vitamin E.<sup>31</sup> Melatonin has been found to be superior to glutathione as well as vitamins C and E in reducing oxidative damage.<sup>6</sup>

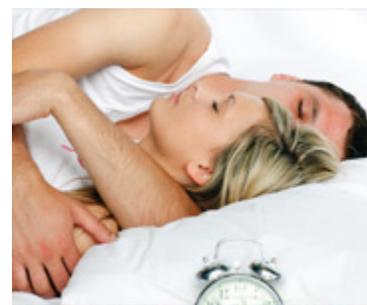
As such a potent antioxidant, melatonin plays a powerful role in fighting free-radical-related diseases—from cardiovascular disease to cancer and practically everything in between.

In post-menopausal women, for example, melatonin has been found to inhibit *lipid peroxidation* (damage to your fat cells caused by free radicals), thus leading to decreased levels of low-density lipoprotein (LDL) cholesterol,<sup>31</sup> one of the primary ingredients for the formation of atherosclerosis. A newer study on men confirmed these findings, suggesting that melatonin leads to overall lower levels of oxidative stress in humans.<sup>32</sup> In individuals undergoing cardiopulmonary bypass surgery, melatonin exhibited a higher reduction in lipid peroxidation and improvements in red blood cell membrane stiffness.<sup>33</sup>

Other widely feared free radical diseases, such as age-related macular degeneration (AMD),<sup>34</sup> acute respiratory distress syndrome (ARDS),<sup>35</sup> glaucoma,<sup>36</sup> and sepsis<sup>37</sup> have also been responsive to increased melatonin levels.

## #2: Melatonin Fights Back Against America's Major Killer

Since cardiovascular disease is the leading cause of death in the United States, melatonin's ability to protect against heart damage is especially noteworthy.<sup>38</sup> In the past decade, melatonin has received considerable attention investigating its potential as a cardioprotective nutrient. Animal studies have provided ample evidence supporting melatonin's antioxidant protection against heart muscle injury,<sup>39,40</sup> reducing the damage done by a heart attack,<sup>41,42</sup> and improving the strength of the heart's pumping action following a heart attack.<sup>43-46</sup>



Other investigators reported that it decreases total cholesterol and LDL levels and increases HDL cholesterol levels.<sup>33,34</sup> Scientists have discovered that individuals with metabolic syndrome have a lower melatonin production rate compared to healthier counterparts without metabolic syndrome and that individuals with metabolic disturbances in blood pressure, cholesterol, and blood sugar management (all classic features of metabolic syndrome) possess lower melatonin levels than those with normal metabolic function.<sup>47</sup> Additional *in-vivo* studies have confirmed that melatonin can lower blood pressure levels.<sup>44-48</sup>

## #3: Cancer Therapy Adjuvant and Immune Regulator

Emerging research suggests that melatonin has *anticarcinogenic* properties—that is, it has the ability to prevent cancer from occurring, or to induce the cancer cell death if it does occur. This has been attributed to melatonin's antioxidant, anti-inflammatory, anti-proliferative, and hormone-modulating properties.<sup>49,50</sup>

Melatonin's ability to interfere with cancer cell multiplication and growth ("proliferation"), as well as inducing cancer cell death ("apoptosis"), has been documented in cancer patients.<sup>51, 52</sup>

It has been successfully used in individuals with advanced stage cancers undergoing conventional anticancer therapy, by either slowing disease progression and/or decreasing treatment side effects.<sup>53-60</sup> In a review of 8 randomized, controlled clinical trials evaluating the benefits of melatonin as an adjuvant therapy for cancer patients with solid tumors undergoing chemotherapy or radiation therapy, researchers found that concurrent use of **20 mg** of melatonin once daily versus conventional treatment alone, improved the rate of complete or partial remission by nearly **50%**, increased the one-year survival rate by **45%**, and decreased the devastating side effects of conventional therapy such as low platelet count, neuropathy, and fatigue by **89%**, **83%**, and **65%** respectively.<sup>59</sup> What's more, these effects were consistent across different types of cancer and there were no adverse events reported.<sup>59</sup>

Melatonin's anticarcinogenic properties can also be attributed to its effect on your immune system. Laboratory studies revealed that melatonin can activate *T-helper cells*, which triggers other immune cells in order to help kill off foreign invaders or pathogens.<sup>61,62</sup> Additionally, melatonin stimulates natural killer cell, monocyte, and macrophage synthesis, and has been found to facilitate healthy cell-to-cell communication, which enhances the body's appropriate immune system response to foreign invaders.<sup>63,64</sup> Based on available evidence, leading experts suggest that patients with cancers and particularly metastatic solid tumors, might benefit from melatonin use, potentially leading to improved therapeutic outcomes.<sup>62-70</sup> Certainly, more research is warranted.

## #4: Protect Against Diabetic Complications

Diabetes—as with cardiovascular disease and cancer—belongs to the family of "free radical disease."<sup>71</sup> Research has found that people with type 2 diabetes and retinopathy experience alterations of their melatonin secretion.<sup>72</sup> Considering the large body of evidence identifying melatonin as a major free-radical scavenger, it is not surprising that preclinical research repeatedly and consistently documents its beneficial antioxidative effects in diabetics and those with high blood sugar

(hyperglycemia).73,74



Melatonin has also been shown to protect pancreatic beta-cells and several diabetes-affected organs (including kidney, retina, brain, and vasculature) from free radical damage.<sup>75</sup> In studies, melatonin treatment has produced reductions in blood glucose, hemoglobin A1c, and cholesterol.<sup>75</sup>

Scientists see great promise for melatonin's potential to improve quality of life by alleviating many of the complications associated with diabetes, such as retinopathy, nephropathy, and

cardiovascular disease.<sup>49,74,75</sup>

#### WHAT YOU NEED TO KNOW: MORE THAN SLEEP; MELATONIN'S MULTIPLE BENEFITS

- Melatonin (*N-acetyl-5-methoxytryptamine*) is a derivative of the amino acid tryptophan and widely distributed in food sources, such as milk, almonds, bananas, beets, cucumbers, mustard, and tomatoes.<sup>21-23</sup>
- In humans, melatonin is primarily synthesized by the pineal gland, but it is also produced in the gastrointestinal tract and retina.<sup>24,25</sup>
- Melatonin and its metabolites are potent antioxidants with anti-inflammatory, hypotensive, cell communication enhancing, cancer fighting, brown fat-activating, and blood-lipid-lowering effects, thereby protecting tissues from a variety of insults.<sup>5-9</sup>
- Melatonin has been shown to support circadian rhythm, hormone balance, reproductive health, cognition, mood, blood sugar regulation, and bone metabolism, while improving overall antioxidant status and lowering blood pressure.<sup>1,10-17</sup>
- Melatonin may assist in preventing diabetic complications, and improving treatment outcomes in patients with cardiovascular disease and certain types of cancer.<sup>1,2,7,9,10</sup>

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### #5: Help Delay Alzheimer's Disease



Another unique and powerful property of melatonin is its ability to cross the blood-brain barrier. Oral intake of melatonin has been shown to increase levels of melatonin in the brain.<sup>76</sup> Melatonin also protects the blood brain barrier particularly in cases of hypoxic injury that may cause increased permeability of the blood brain barrier and lead to more damage to the delicate brain tissue as compounds that normally would be kept out by a functioning blood brain barrier gain entrance to the brain.<sup>77</sup> Intensive research over the past decade has indicated melatonin's beneficial effects in experimental models of neurodegenerative disorders, specifically those linked to oxidative damage.<sup>78</sup> In fact, melatonin's broad spectrum

antioxidant activity in many central nervous system neurodegenerative diseases has been well-documented and reviewed.<sup>78,79</sup>

Specifically, melatonin can help delay the onset of Alzheimer's disease (AD) and help protect vital cellular structures, such as mitochondria, from oxidative damage and decay.<sup>80</sup> Declines in mitochondrial function are a hallmark feature of many neurodegenerative diseases including Alzheimer's disease, Parkinson's disease, and Huntington's disease.<sup>81</sup> Melatonin may

also promote improved sleep patterns and prevent cognitive impairment and improve the confusion and restlessness that often occurs in the evening (called *sundowning*) in AD patients.<sup>80,82,83</sup> Preclinical studies revealed that melatonin exerts pronounced neuroprotective effects against *beta amyloid plaque*, one of the specific underlying causes of Alzheimer's disease.<sup>84-86</sup>

More recent investigations show that melatonin may prevent brain cell death while maintaining energy and oxygen metabolism in highly stressed neuronal mitochondria.<sup>87,88</sup> Interestingly, decreased night time melatonin levels have been associated with the severity of mental impairment in dementia patients, and disturbed circadian rhythms seem to be correlated with cognitive performance in elderly and Alzheimer's patients.<sup>81,89,90</sup> It is important to note that while melatonin may prove beneficial in earlier stages of Alzheimer's disease, it is much less effective in late stage Alzheimer's and may fail to improve sleep or agitation.<sup>92,93</sup>

## #6: Combat Obesity with Melatonin

In recent years, dietitians and medical experts have recognized that obesity is often associated with stress, emotional eating, sleep-deprivation, and hormonal changes later in life. A recent study in women with *night eating syndrome* (an eating disorder characterized by late-night binge eating) added further confirmation to this. It found that women suffering from this disorder had pronounced circadian melatonin rhythm disturbances, which also affected levels of *cortisol* (a stress hormone that can be a factor in weight problems) and *ghrelin* (a hormone that stimulates hunger). It also affected a variety of other behavioral and physiological circadian markers involved in appetite and neuroendocrine regulation.<sup>94</sup>

While no human weight-management trials using melatonin have been published thus far,<sup>95</sup> preclinical trials are encouraging. In middle-aged rodents, daily melatonin administration was found to suppress abdominal fat, plasma leptin levels, and insulin levels, while also reducing body weight and food intake.<sup>96,97</sup> Other researchers reported that melatonin was associated with decreased intra-abdominal fat, decreased plasma insulin and leptin levels, and the absence of age-related weight gain.<sup>95,98</sup>

Furthermore, laboratory investigations discovered melatonin's ability to activate brown adipose tissue, which encourages your body to burn fat instead of storing it.<sup>99-101</sup> In recent years, brown fat has increasingly become a target for halting the global obesity epidemic.<sup>102</sup> In a rat model of pre-diabetic, diet-induced obesity, supplementing obese rats with 4mg/kg/day of melatonin resulted in reductions in body weight, belly fat, serum insulin levels, and triglycerides.<sup>103</sup> In humans, the equivalent dose is **48 mg** for a 165 lb adult, which is a very high dose that could produce next day drowsiness. Typical human doses for melatonin range from **300** micrograms to **10** milligrams at bedtime.

## #7: Help Prevent Osteoporosis

Data derived from animal research suggests that melatonin has beneficial effects on bone repair and remodeling, and bone mineral density,<sup>104</sup> which would make it an ideal candidate for the prevention of osteoporosis or as adjuvant after bone fractures.

A very small, yet compelling recently published double-blind, placebo-controlled pilot study investigated the effects of melatonin on bone health and quality of life in 18 perimenopausal women (ages 45-54) for 6 months. It found that melatonin improved physical symptom scores (e.g., feeling and sleeping better), increased *osteocalcin* (a marker for bone formation), and decreased levels of *Type-I collagen cross-linked N-telopeptide* (a marker for bone resorption), indicating that melatonin may restore imbalances in bone remodeling and prevent bone loss.<sup>105</sup>

However, while the results from this small study appear clinically relevant, further investigation is warranted.



## Summary

Aging is a multi-factorial process, involving a heavy load of free radicals, metabolic, hormonal, and changes in immunity. Although there is currently no direct clinical evidence demonstrating that melatonin may prolong the human life span, there are several reasons to postulate its role in the aging cascade:

- Melatonin participates in many vital life processes, and its secretion falls gradually over time.
- Diminished melatonin levels appear to correlate with the deterioration of many metabolic functions and decreasing hormone levels, thus possibly contributing to the acceleration of aging processes.
- Melatonin exhibits immunomodulatory properties; suppressed immunity has been implicated in the acceleration of aging processes.
- Melatonin has remarkable low toxicity and is without significant side effects if used at <10 mg/day (provided as 'regular' or 'fast-release');106

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