

Melatonin and its Health Benefits

1. Introduction and 'Age-related biological changes and increased life span' to 'Infertility'

If, after reading this article, you feel you would like to boost your levels of melatonin, EMFields stocks a supplement containing [pure melatonin](#) and [one which contains grass extracts](#) high in natural melatonin.

Melatonin, or 5-methoxy-N-acetyltryptamine, is a hormone found in all living creatures, including plants (Reiter [2007](#), Paredes [2009](#)), at levels that vary in a daily cycle.

A study by Burgess & Fogg ([2008](#)) found that in the 170 people they studied, lifestyle and behavioural variables were only able to explain about 15% of the individual variability in the amount of melatonin secretion, the rest of which they attributed to a substantial genetic influence.

Melatonin, and its by-products (Reiter [2008](#), Millán-Plano [2010](#)) are extremely powerful antioxidants with a particular role in protecting DNA. It reduces experimental cataractogenesis, traumatic injury to the spinal cord and brain, and protects against oxidative damage to neurons and ganglia in models of stroke, Parkinsonism and Alzheimer's disease (Reiter [2008](#)). It is naturally synthesized from the amino acid tryptophan via synthesis of serotonin. Melatonin is also essential for glucose homeostasis and regulation (Kedziora-Kornatowska [2009](#)). Reiter [1997](#), Ximenes ([2009](#)), Makay ([2009](#)) propose mechanisms by which melatonin's anti-oxidant properties may be explained. Lai & Singh ([1997](#)) found that melatonin blocked radio-frequency induced DNA damage in the brain cells of rats, which could lead to neurodegenerative diseases or cancer.

Melatonin represents one of the most important immune system enhancing substances in our body, and, as a free radical scavenger, protects all body and brain cells against genetic damage considered to be a precursor to cancer (Gulcin [2008](#)). Serotonin acts as a messenger for the nervous system and in the brain as a mood hormone. A reduced serotonin level is associated with depression, lethargy and listlessness, inner agitation and many psychiatric disturbances.

Melatonin regulates chronobiological and reproductive systems and mammary gland functions. As well as the properties mentioned above, melatonin's other functions include body weight control and the promotion of wound healing, the coupling of environmental cues to circadian clock gene expression and the modulation of secondary endocrine signalling (e.g. prolactin release, oestrogen receptor-mediated signalling). Mammalian skin and hair follicles are not only melatonin targets, but also sites of extrapineal melatonin synthesis (Slominski [2002](#), Fischer [2008](#)). Geomagnetic activity may play a role in the entrainment of melatonin rhythms (Burch [2008](#)).

Melatonin (as well as 3 other hormones, which are also implicated in antitumour action - Lissoni [2003](#)) is produced primarily in the pineal gland, which is located in the brain, and the production is dependant on the light-dark cycle, being produced primarily during the night. Secretion of melatonin, and its level in the blood, peaks in the middle of the night, and gradually falls during the second half of the night, with normal variations in timing according to the individual. However, melatonin is also produced in different cells and tissues from the immune system (Gómez-Corvera [2009](#)). Melatonin is also produced to a lesser extent, in the bone marrow cells, lymphocytes and epithelial cells. Melatonin concentration in these cells is much higher than that found in the blood but it does not seem to be regulated by the photoperiod.

It has been suggested that older people wake at a time when they have higher melatonin levels than younger people, as a result of an advance in sleep timing and circadian melatonin rhythm associated with age (Duffy [2002](#)).

Melatonin levels in the first morning urine excretion are strongly correlated with total nocturnal plasma melatonin output and peak nocturnal melatonin values and therefore is a reasonably reliable, easy method of determining melatonin levels in women aged 40-70 (Cook [2000](#)).

Some foods and drink help increase melatonin consumption; red wine, bananas, oats, fruit vegetables and cereals. Melatonin is present in many plants, possibly to protect against UV light. Purslane has 10-20 times more melatonin than any other edible plant, followed by St John's Wort, sage and feverfew. If taken as a supplement, melatonin should be taken at night-time to promote the normal circadian rhythms.

The peak production time of melatonin can be shifted by careful environmental manipulation to increase its production in night shift workers. Some of these changes include intermittent bright light pulses during night shifts, wearing dark glasses when outside, sleeping in dark bedrooms at scheduled times after night shifts and on days off, and receiving outdoor light exposure upon awakening from sleep (Smith [2008](#)). These changes helped study subjects to perform better than their colleagues on a reaction time task.

The circadian secretion of night time melatonin begins at the approximate age of 4 months. For this purpose, nursing according to the day-night light-dark cycle is essential right from early infancy (Segawa [2008](#)).

Once you pass 65, your body will be able to make only about 10% of the melatonin you did when you were 30, although this is disputed by some researchers, assuming a good general state of health (Zeitler [1999](#)). Davanipour ([2009](#)) suggests that low levels of endogenous melatonin production among older individuals may lead to higher levels of DNA damage, possibly increasing the risk of cancer.

Li ([2008](#)) suggested that the beneficial effects of electroacupuncture which protects the brain from ischemic damage (stroke effects) may be related to its effect on melatonin changes.

Age-related biological changes and increased life span

Ageing has been proposed as the major risk factor in most neurodegenerative disorders. Studies by Akbulut ([2008](#)) and García ([2010](#)) concluded that exogenous melatonin had a potential role for retardation of age-related oxidative events. Oztürk ([2008](#)) found melatonin increased levels of Zinc, which reduces with age, in some parts of the body. Magnanou ([2009](#)) found that continuous melatonin administration delayed the onset of senescence. Esteban's study ([2010](#)) of melatonin treatment of aged rats believes that it may improve the age-dependent deficits in cognition and motor function.

Melatonin has been shown to increase the average life span of mice by 20% in some studies (Oaknin-Bendahan [1995](#), Anisimov [2003](#), Rodriguez [2007](#)). It restored some of the ageing effects in mice (Morioka [1999](#), Okatani [2002](#), [2003](#), Gutierrez-Cuesta [2008](#)).

Alcohol-induced damage

Melatonin and vitamin C administration provided partial protection against alcohol-induced oxidative stress (Sönmez [2009](#)).

Asthma

People who are asthmatic at night may have higher than normal melatonin levels. This may indicate an adverse effect of melatonin for people with this condition. (Sutherland [2002](#), [2003](#), [2005](#)).

Autism

People who suffer from autism have half as much melatonin in their blood as the rest of the population. This may be exacerbated by their irregular sleep patterns, which prevent their bodies from making the hormone efficiently. Melatonin administration was found to be promising as an efficient and safe treatment of severe sleep disturbances in adults with autism (Galli-Carminati [2009](#)).

Behaviour

Melatonin treatment in persons with intellectual disability and chronic insomnia decreases daytime challenging behaviour, probably by improving sleep maintenance or by improving circadian melatonin rhythmicity (Braam [2010](#)).

Blood Brain barrier

Melatonin can easily cross cell membranes and the blood-brain barrier (Hardeland [2005](#)).

Blood flow (restriction and restoration)

Maternal melatonin administration appeared to prevent problems with bloodflow and DNA damage in the foetal rat brain (Wakatsuki [1999](#), [2001](#), Watanabe [2004](#)), and prevented placental DNA damage and foetal growth restriction (Nagai [2008](#)). Melatonin also reduced cerebral vasospasm (Aladag [2009](#)).

Melatonin also prevented liver tissue (Okatani [2003](#)) testicular (Duru [2008](#)) and kidney damage (Ersoz [2009](#)) due to restricted, then restored, blood flow.

Brain damage

There are mixed results as to the effectiveness of melatonin after intracerebral haemorrhage. One study (Hartman [2008](#)) found no effect, whereas Rojas ([2008](#)) found melatonin reduced oxidative stress, but it did not change the extent of brain oedema or neurologic deficits.

Melatonin was found to reduce oxidative damage in the brain caused by exposure to mobile phone radiation (Sokolovic [2008](#)).

Birth asphyxia is associated with disturbed development of the neonatal brain. Melatonin was found to be effective in helping prevent brain injury at birth due to insufficient oxygen, and the authors (Hutton [2009](#)) suggested that the prophylactic administration of melatonin in the last few days before delivery may help prevent such damage. Kaur ([2010](#)) also found that melatonin reduced hypoxic damage to the neonatal brain, due, they hypothesised to its antioxidant properties.

Cancer

Melatonin is a particularly powerful antioxidant, 5 times more potent than vitamin C, which acts as a natural anti-cancer agent in the body ([Sánchez-Barceló 2003](#), Pauley [2004](#)). Danielczyk & Dziegiel ([2009](#)) suggest that melatonin may be a useful therapeutic approach in human cancer prevention.

It is highly protective of oxidative damage to human blood cells (Vijayalaxmi [1995](#), [1996](#), [1999](#), [Badr 1999](#), [Juutilainen 2006](#)) - the sort of damage that could lead to leukaemia ([Blackman 2001](#), [Henshaw 2005](#)), and can prevent damage to DNA (Karbownik [2001](#)).

Srinivasan ([2008](#)) commented that *"In addition to its direct oncostatic action, melatonin protects hematopoietic precursors from the toxic effect of anticancer chemotherapeutic drugs. Melatonin secretion is impaired in patients suffering from breast cancer, endometrial cancer or colorectal cancer."*

Cucina ([2009](#)) and Girgert ([2009](#)) found that melatonin killed MCF-7 **breast cancer** cells. Benitez-King ([2009](#)) found that melatonin is able to switch microfilament phenotypes in MCF-7 human mammary cancer cells from invasive migratory cells to dormant microfilament phenotypes. In a paper as long ago as 1990 Kerenyi, discussing the role of the pineal gland (and subsequent serum melatonin levels), proposed that melatonin may have a direct effect on breast tumours, especially oestrogen-dependent tumours (Kloog 2008, Viswanathan & Schernhammer [2008](#), Maganhin [2008](#)), the melatonin receptors being the probable sites of interaction between melatonin and the tumour cell. Grant commented ([2009](#)) *"Melatonin works through receptors and distinct second messenger pathways to reduce cellular proliferation and to induce cellular differentiation. In addition, independently of receptors melatonin can modulate oestrogen-dependent pathways and reduce free-radical formation, thus preventing mutation and cellular toxicity"*.

In a review of potential mechanisms, Korkmaz ([2009](#)) proposes that 1) melatonin influences the regulation of breast cancer cell growth 2) melatonin down-regulates the expression of genes responsible for the local synthesis or activation of oestrogens 3) melatonin inhibits telomerase activity and expression induced by either natural oestrogens or xenoestrogens 4) melatonin modulates the cell cycle through the inhibition of cyclin D1 expression 5) melatonin influences circadian rhythm disturbances with the subsequent deregulation of PER2 which acts as a tumour suppressor gene.

It seems that premenopausal women's risk of developing breast cancer may be inversely related to overnight melatonin production (Schernhammer [2010](#)).

Merklinger-Gruchala ([2008](#)) reported that sleep variation may influence endogenous oestrogens, and therefore risk of breast cancer. An estimated 45-80% of breast cancer patients use antioxidant supplements after diagnosis, and the use of antioxidant supplements during breast cancer treatment is common. In a review of 22 articles, Greenlee ([2009](#)) suggested that melatonin could enhance tumour response during treatment, but that the trials did not have sufficient statistical significance to be conclusive.

It may be that people may sleep less when their work patterns are different. Some research (Verkasalo [2005](#), Kakizaki [2008](#), Wu [2008](#)) though not all (Pinheiro [2006](#)), has shown a decreased risk of breast cancer and prostate cancer (Kakizaki [2008](#)) in long sleepers, possibly because of its effect on melatonin levels.

Joo & Yoo ([2009](#)) suggested that melatonin may be promising for anti-prostate cancer strategies due to its ability to induce apoptotic death.

Cardiovascular support

Melatonin may play a role in preventing cardiac arrhythmia.

A Russian review of the literature found evidence of therapeutic effects of melatonin in the treatment of arterial hypertension and cardiac ischemic disease (Russian a [2008](#)). Petrosillo ([2009](#)) and Diez ([2009](#)) found that melatonin protected the heart from reperfusion injury.

Grossman ([2006](#)) and Reiter ([2008](#)) found that melatonin supplementation may be an effective treatment for hypertension. Oral melatonin seemed to have the effect of reducing systolic blood pressure in one small study (Yildiz [2006](#)). The same author found that increased levels of melatonin during the night were found to cause decreased blood pressure and heart rate (Yildiz [2009](#)).

Nicotine exposure depletes myocardial antioxidant enzymes and increases free radicals and lipid peroxidation products. Baykan ([2008](#)) found that melatonin prevents the nicotine-induced cardiac injury.

A review of studies identifying edible plants displaying cardioprotective properties after chemotherapy, found that melatonin could be a safe and effective way of alleviating anticancer chemotherapy and preventing heart failure (Piasek [2009](#)).

Central Nervous System (CNS) injuries and diseases

Das ([2010](#)) found that melatonin may be an effective neuroprotective agent to attenuate motoneuron death in CNS injuries and diseases.

Dementia

Melatonin helped reduce the severity of Alzheimer's disease (Rodriguez [2007](#), Masilamoni [2008](#)) and slowed its progression (Olcese [2009](#)). Rodriguez suggested that melatonin's antioxidant abilities may help reduce the inflammation and free radical damage in the brain. Melatonin prevented cell damage in a laboratory study (Hoppe [2010](#)), causing the authors to speculate that it "may provide an effective therapeutic strategy for Alzheimer's disease".

A study by Dowling ([2008](#)) found that the combination of bright but not constant light (Ling [2009](#)), and melatonin could slow the progression of dementia. There was also a change in activity levels from night time to day time which would result in an easier management regimen for carers.

Gunasingh ([2008](#)) suggests that melatonin may be a potential therapeutic agent in the prevention of oxidative stress associated with Abeta and Alzheimer's disease, it can also prevent dopamine turnover induced by Abeta.

Depression, bipolar disorder and mood control

Serotonin, from which melatonin is derived, is involved in mood control and changes in melatonin levels may be the mechanism underlying the links between EMFs and chronic fatigue, depression and suicide.

The occurrence of disturbed sleep is one of the principal diagnostic criteria for major depressive disorder (MDD). There is evidence of reciprocity between the two conditions such that, even in

the absence of current depressive symptoms, disturbed sleep often predicts their development. It has been suggested that the recently introduced novel melatonin agonist has been very effective in improving the mood of depressed patients because of its ability to improve sleep quality. The use of melatonin is a promising treatment for depression (Rahman [2009](#), Pandi-Perumal [2009](#), Serfaty [2010](#)). Agomelatine, a novel melatonergic antidepressant has been shown to improve sleep in depressed patients and to have an antidepressant efficacy that is partially attributed to its effects on sleep-regulating mechanisms (Srinivasan [2009](#)).

A Turkish study (Ergün [2008](#)) found that the co-administration of the antidepressant imipramine together with melatonin was better than either separately at ameliorating the symptoms of depression, depending on dosage, and there was no interaction between the drugs.

Rats chronically exposed to short daylight or to melatonin regimen mimicking short daylight, showed anxiety- and depression-like behaviours (Ashkenazy [2009](#)). It is important that exposure to daylight is part of everyone's daily rhythm, especially people who work primarily in conditions of artificial light which has a different spectrum to that of natural daylight. An antidepressant drug structurally similar to melatonin, improved sleep without causing daytime sedation, sexual or cardiac adverse effects, weight gain or discontinuation syndromes (Dubovsky & Warren [2009](#)).

Dallaspezia & Benedetti ([2009](#)) say *“Chronotherapeutic strategies based on controlled exposures to environmental stimuli that act on biological rhythms have shown good efficacy in the treatment of illness episodes”*.

Lewy ([2009](#)) in a recent review, also acknowledges that many, if not all, mood disturbances have a circadian misalignment component of the phase-delay type, which can be treated with bright light in the morning and/or low-dose melatonin in the evening.

Diabetes

An experiment by Gül ([2008](#)) found that the administration of melatonin reduced corneal injury in diabetic rats. Kedziora-Kornatowska ([2009](#)) found an improvement of antioxidative defense after melatonin supplementation in people with non-insulin dependent diabetes mellitus (NIDDM), and suggest melatonin supplementation as an additional treatment for the control of diabetic complications, especially in the elderly. A diabetic woman, treated with phototherapy, which increased her melatonin secretion, required less insulin (Nieuwenhuis [2009](#)).

A low dose of melatonin was found to be effective in reducing hepatic oxidative stress in diabetes (Shaker [2009](#)).

Drug dependency

In an experiment on morphine-induced conditioned ‘place preference’ in mice, injected melatonin was found to reverse the effect (Han [2008](#)).

Drug interaction

Kidney damage is a major complication of acetaminophen (APAP), a widely used analgesic and antipyretic drug. Ilbey ([2009](#)) found that administration of melatonin protected against APAP-induced kidney damage.

The effect of a cancer suppressor drug (Celecoxib) was enhanced when melatonin was given in combination (Orendas [2009](#)).

Eye problems

In one study (Sande [2008](#)), melatonin was found to prevent the clinical, biochemical, histological, ultrastructural and functional consequences of experimental uveitis (inflammation of the interior of the eye).

Oral melatonin premedication for patients undergoing cataract surgery under topical anesthesia was found by Ismail & Mowafi ([2009](#)) to provide anxiolytic effects, enhanced analgesia and decreased intraocular pressure resulting in good operating conditions.

Melatonin had a protective effect on retinal pigment cells against induced oxidative damage. The mechanism possibly involved reinforcing the cell viability, strengthening the activity of antioxidase, and reducing apoptosis (Xu 2009).

Fibromyalgia

Fibromyalgia is a painful syndrome, that is experienced by many people as a precursor to ES. It has been suggested that melatonin supplementation may be effective in treating the pain associated with fibromyalgia, as well as addressing the sleep problems common in this syndrome (Reiter [2007](#)).

Headaches

Melatonin was found to decrease the number of headaches suffered by children. In 14 out of 21 children headaches had reduced by 50% and 4 children had had no headaches at all after 3 months (Miano [2008](#)).

Immune system effects

While it is clear that melatonin interacts with the immune system (Arushanian [2002](#), Carrillo-Vico [2005](#)), the details of those interactions are unclear. There have been few trials designed to judge the effectiveness of melatonin in disease treatment. Most existing data are based on small, incomplete, clinical trials. Sirajudeen ([2011](#)) found improved immune responses and other cellular changes in chicks after melatonin was added to their water, though another study had found this was an age-dependent effect (Sharman [2008](#)). Zhou ([2009](#)) found that melatonin promoted the proliferation of neonatal cord blood mononuclear cells and peripheral blood mononuclear cells and thus enhanced the lymphocyte immune system.

Sirajudeen's team felt that long-term rather than short-term administration of melatonin was more effective at reducing toxicity.

Cernysiov ([2010](#)) found that antibodies significantly decreased in mice exposed to light and daily melatonin treatment brought the antibody level back to normal.

Infertility

Serum and seminal plasma melatonin levels have been found to be significantly low in infertile males (Awad [2006](#)).

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