

Melatonin and its health benefits

2. 'Inflammatory conditions' to 'Ventilator-induced lung injury'

Inflammatory conditions

It has been suggested (Maldonado [2009](#)) that melatonin could exert a regulatory effect on inflammatory conditions which are mediated by mast cells.

Irritable Bowel Syndrome (IBS) and other gastric problems

It was found that melatonin may be a promising candidate for the future research of agents that can modulate bowel motility and other IBS symptoms, in two studies by Lu ([2005](#), [2009](#)).

Gastric ulceration can be induced in rats by an administration of 15% hydrogen peroxide. Mohamadin ([2009](#)) found that the administration of melatonin 30 minutes before the hydrogen peroxide reduced the development of gastric lesions. The higher the dose, the greater the reduction.

Melatonin pretreatment significantly reduced haemorrhagic lesions and decreased oesophageal lipid peroxidation aggravated by Reflux Esophagitis (RE). Melatonin's free radical scavenging properties and antioxidant effects resulted in the improvement of oesophageal defence mechanisms (Lahiri [2009](#)).

Oral melatonin was found to be promising for the treatment of gastro-oesophageal reflux disease (GERD) (Kandil [2010](#)), also relieving epigastric pain and heartburn.

Melatonin was found to reduce gastric damage caused by treatment with NSAIDs (Maity [2009](#)).

Kidneys

Melatonin treatment had a protective effect on kidney damage induced in rats by 900 MHz phone radiation (simulating the sort of damage that can occur by attaching a mobile phone on standby to the belt) (Oktem [2005](#)).

Acute renal dysfunction is a frequent complication after cardiac surgery with cardiopulmonary bypass (CPB). Melatonin was effective in preventing CPB-induced renal damage (Wang Z [2009](#)).

Melatonin also reduced the cortisol response to adrenocorticotrophic hormone (ACTH), suggesting a direct melatonin action on the adrenal gland Campino ([2008](#)).

Liver damage

Melatonin was found to protect against damage to the liver induced by carbon tetrachloride in rats (Hong [2009](#)).

A high dose of melatonin was found to have an antiproliferative effect on hepatoma cells (Ozdemir [2009](#)). Used together with Doxorubicin, hepatoma cell growth was inhibited and the combination induced cell apoptosis (Fan [2010](#)).

Malaria

Melatonin has been found to have a two-pronged effect on malaria development. Firstly melatonin agonists can prevent the maturation of the parasites responsible for malaria, and melatonin administration at high dosages can be used to inhibit apoptosis and liver damage resulting from the oxidative stress in malaria (Srinivasan [2010](#)).

Menopause

Oxidative stress has been proposed to explain the biological side effects of experimental menopause. Melatonin prevented Oxidative stress in ovariectomized rats (Dilek [2010](#)).

Mouth diseases

Melatonin, which is released into the saliva, may play a role in protecting the oral cavity (periodontal diseases, herpes viral infections and Candida, oral ulcers and oral cancer) from tissue damage caused by oxidative stress (Gómez-Moreno [2010](#), Srinath [2010](#)).

Neurocognitive functions

In a review of studies, melatonin has been found to maintain neurocognitive functions after irradiation (Manda [2009](#)).

Neurodegenerative diseases, such as Huntington's disease

Results of the study by Tasset ([2009](#)) supported the hypothesis that melatonin could be useful in the treatment of diseases such as Huntington's disease, possibly by reducing oxidative stress.

Nitric oxide interaction

Yariktas ([2005](#)) found that exposure to a 900 MHz source increased nitric oxide (NO) levels in the sinus and nasal mucosa. They suggested that increased NO levels may act as a defence mechanism and relate to tissue damage. Melatonin seemed to have a beneficial effect preventing the changes in the mucosa.

Operation trauma

Melatonin was found to reduce post-operative delirium in children, though it did not reduce pre-operative anxiety (Kain [2009](#)).

Intra-abdominal adhesions are important postoperative complications following abdominal surgery. Melatonin significantly reduced adhesion formation (Ersoz [2009](#)).

Preoperative oral melatonin administration decreased pain scores and tramadol consumption and enhanced sleep quality, sedation scores, and subjective analgesic efficacy during the postoperative period (Borazan [2010](#)). Mowafi & Ismail ([2008](#)) found similar effects.

Ovarian disease

Melatonin could become an important medication for improving ovarian function and oocyte quality and open new opportunities for the management of several ovarian diseases (Tamura [2009](#)).

Pain relief

A review of papers (Ambriz-Tututi [2009](#)) investigating the role of melatonin in pain relief concluded that melatonin receptors could prove attractive targets for developing analgesic drugs, including for the more difficult to treat neuropathic pain states.

Pancreatitis

Melatonin helped prevent oxidative damage in acute pancreatitis (Col [2010](#)), and was found to promote the spontaneous regeneration process of pancreatic tissue (Sidhu 2010).

Parkinson's disease

Rodriguez ([2007](#)) at the University of Granada in Spain suggested that the melatonin's antioxidant abilities may help reduce the severity of Parkinson's which involves inflammation and free radical damage in the brain.

The antioxidant activity of melatonin may reduce damage caused by some types of Parkinson's disease. A Ukrainian study (Talanov & Sahach [2008](#)) found that melatonin blocked the mitochondrial pore openings in nerve cells, helping to prevent neurodegeneration.

Plants

It was found (Chen [2009](#)) that melatonin applied to seedlings stimulated root growth. There were significant windows of dose and seedling age, and had no effect or even an inhibitory effect when given outside these windows.

Pregnancy and reproduction

Human melatonin has an important influence on the female genital system. In fact, melatonin may influence production and action of steroids, modifying cellular signalization on the target tissue (Maganhin [2008](#)).

Daytime melatonin levels in normal pregnancies are low. Night-time melatonin levels increase after 24 weeks gestation, with significantly high levels after 32 weeks. These values decrease to non-pregnant levels on the second day after birth. Night-time melatonin levels are even higher in twin pregnancies after 28 weeks gestation. Patients with severe preeclampsia had significantly lower melatonin levels than the women with mild preeclampsia or normal pregnancies after 32 weeks gestation (Nakamura [2001](#)). Melatonin protects against oxidative damage in the placenta caused by restriction of blood flow. It could be useful in treating preeclampsia and possibly other clinical states involving excess free radical production, such as foetal growth restriction and foetal hypoxia (Okatani [2001](#)).

In an experiment by Fujinoki (2008) melatonin was found to enhance sperm hyperactivation in hamsters, and du Plessis (2010) found that the application of melatonin showed a significantly higher percentage of motile progressive motile and rapid cells in human spermatozoa, through a direct or indirect effect on the antioxidant scavenging effect of NO.

Exposure to 16 hours of light per day, followed by melatonin treatment improved the semen characteristics of male goats, especially during the breeding season (Ramadan 2009).

Melatonin had beneficial effects on the *in vitro* development of 2-cell mouse embryos (Tian 2010). Whether this applies to human foetal development is unclear as mice can be quite different.

Radiation side effects

The small intestine is the most radiosensitive gastrointestinal organ and patients receiving radiotherapy directed to the abdomen or pelvis may develop radiation enteritis (Hussein 2008).

Administration of melatonin, or AFMK, a melatonin metabolite, prior to irradiation can protect against the destructive effects of X-rays (Manda 2007, Reiter 2008). Manda (2009) found that melatonin pretreatment combated the delayed side effects of cranial radiotherapy. Shirazi (2007) suggested not only that melatonin was useful in helping prevent accidental damage to cells in proximity to target cells, but that it may be a useful radioprotector for radiation workers.

Vijayalaxmi, in a review of melatonin as a radioprotective agent (2004) concluded that it may have a use in protecting individuals from radiation terrorism.

Scoliosis

Melatonin deficiency plays a role in the prognosis of idiopathic scoliosis (Machida 2009). The authors suggest that melatonin supplements may prevent the progression of scoliosis, especially in mild cases with less than a 35 degree curve.

Skin effects

Melatonin is a major skin protectant and its functions may impact on skin biology and pathology (Fischer 2008). It has also been found to reduce the effect of burns (Bekyarova 2009) and mobile phone radiation (Ayata 2004).

Melatonin has been found to protect melanoma cells against both UVA and UVB radiation (Izykowska 2009).

Sleep

The levels of melatonin in the body rise in the evening and this increase promotes the ability to fall asleep. Melatonin supplementation has been associated with an improved ability to get to sleep and also to stay asleep. This has long been known to sufferers of jet lag, who synchronise their body clocks by the judicious use of melatonin to re-assert proper sleeping habits. Melatonin was found to be an effective and well-tolerated treatment for insomnia in paediatric patients with Attention-Deficit/Hyperactive Disorder (ADHD) (Benz & Scates 2010), autism and/or fragile X syndrome (Wirojanan 2009). The Food and Drug Administration in America has approved a drug containing melatonin and it is prescribed for the treatment of insomnia in children and the elderly (Reynoldson 2008). Any disruption in the quality of sleep with the accompanying cellular repair processes will clearly impact on many areas of health.

In adults with chronic insomnia, long term treatment with a melatonin-based medication, ramelteon, reduced sleep onset time and promoted sleep with no residual effects, rebound insomnia or withdrawal symptoms upon discontinuation (Mayer [2009](#), Srinivasan [2009](#)). Srinivasan suggested that melatonin promotes sleep by regulating the sleep/wake rhythm through the action on melatonin receptors in the suprachiasmatic nucleus (SCN). Wade & Downie ([2008](#)) suggested that melatonin significantly improved morning alertness and quality of sleep.

Sleep is a thalamic function and it is assisted by melatonin which acts by promoting spindle formation. In this way, melatonin has a modulatory influence on sleep onset and maintenance (Jan [2009](#)).

Melatonin supplements improved sleep patterns in an experiment where awareness of the time of day was withheld, and an artificial 20-hour day was imposed, and the normal melatonin secretion was out of phase (Wyatt [2006](#)).

Melatonin offers functional and metabolic protection in cases of intermittent hypoxia (IH), which is important to reduce pathological changes as a result of obstructive sleep apnea (OSA) (Bertuglia & Reiter [2009](#))

Stress

A melatonin-based antidepressant was found to block the adverse effects of stress on memory (Conboy [2009](#)). Melatonin levels were found to be higher in children with acute stress (traumatic, surgical, psychic or febrile) or reduced in instances of chronic stress (Muñoz-Hoyos [2009](#)). The authors concluded *"The lack of an appropriate response to acute stress could make some groups of patients predisposed to suffer depressive symptoms associated with a wide range of neurological, endocrinological or immunological consequences."*

Stroke

Koh ([2008](#)) and Sung ([2009](#)) found that melatonin prevented cell death resulting from ischemic brain injury and suggested the most likely mechanism by which this was occurring. Wang X ([2009](#)) also demonstrated that melatonin, together with methazolamide was neuroprotective against cerebral ischemia, due to their ability to cross the blood-brain barrier and provide a mitochondrial-based screen. Ritzenthaler ([2009](#)) and Ahmad ([2010](#)) concluded that melatonin could have neuroprotective effects. Melatonin prevented vasospasm after subarachnoid hemorrhage (a type of stroke) and reduced arterial inflammation and oxidative stress (Fang [2009](#)).

Testicular protection

Pre-treatment and post-treatment with high-dose melatonin both significantly alleviated carbon ion-induced acute testicular damage, a greater radioprotective effect being observed in the pre-treatment group (Liu [2009](#)).

Toxin Protection

Melatonin was found to protect against damage from formaldehyde-induced oxidative renal damage and neurotoxicity (Zararsiz [2007](#)), tetrachloride-induced changes (Ogeturk [2004](#), Aranda [2010](#)) arsenite-induced peripheral neuropathy (Lin [2009](#)), deltamethrin (pesticide) induced nerve cell damage (Guo [2008](#)), mitomycin C induced genotoxicity (Ortega-Gutiérrez [2009](#)) and 2-Bromopropane-induced testicular toxicities (Huang [2009](#)). Alonso-Gonzalez ([2008](#)) found that melatonin helped prevent cancers that were a result of cadmium contamination, and El-Sokkary

(2010) confirmed its antioxidant qualities in combatting cadmium toxicities. In a review of the effects of melatonin, Reiter (2008) found that it ameliorated the extensive free radical-mediated damage that ensued following exposure to a wide variety of environmental insults, including toxic prescription drugs, neural toxins, herbicides and metals.

Ventilator-induced lung injury

Melatonin decreases ventilator-induced lung injury by increasing the anti-inflammatory response in spite of an unexpected increase in oxidative stress (Pedreira 2008).