Melatonin and Health Benefits

This article is separated into 5 sections, each of which can be individually downloaded. It is a 'work in progress' incorporating new information whenever time permits.

Section 1

Age-related changes to Dementia

1. Introduction; Age-related biological changes and increased life span; Alcohol-induced damage; asthma; autism; behaviour; bladder; blood-brain barrier; blood flow; blood pressure; brain damage; burns; cancer; cardiovascular support; Central Nervous System (CNS) injuries and diseases; chemical; dementia

2. Depression, bipolar disorder and mood control; diabetes, diabetic retinopathy; DNA damage; drug dependency; drug interaction; eye problems; fibromyalgia; headaches; head injury; height; immune system effects; infertility; inflammatory conditions; Irritable Bowel Syndrome (IBS) and other gastric problems; kidneys; learning and memory; light at night; light pollution; liver damage; lung injury; malaria; menopause; metabolic disorders; mitochondrial dysfunction; mouth diseases; nerve damage; neurocognitive functions; Neurodegenerative diseases, such as Huntington's disease; neurodevelopmental disorders; nitric oxide interaction; obesity

3. Operation trauma; ovarian disease; pain relief; pancreatitis; Parkinson's disease; plants; pregnancy and reproduction; radiation side effects; schizophrenia; sciatic nerve injury; scoliosis; skin effects; sleep, sleep apnoea; spinal cord injury; stress; stroke; testicular protection; thyroid; toxin protection; treatment side effect reduction; vaccinations; ventilator-induced lung injury; Wi-Fi

4. Melatonin suppressors: Alcohol; age; baby crying; cancer; chemicals; diet; weight; electromagnetic fields (EMFs), powerfrequency radiation; occupational radar exposure; radiofrequency radiation; light; light at night (LAN); light wavelength; smartphone; fracture risk

5. References – 467 references

Melatonin and its Health Benefits
1. Introduction and 'Age-related biological changes and increased life span' to 'Dementia'

Melatonin, or 5-methoxy-N-acetyltryptamine, is a hormone found in all living creatures, including plants (Reiter 2007, Paredes 2009), at levels that vary not only in a daily cycle, but also in a solar cycle, with year -to-year variations. Nocturnal melatonin increased in the summer, depending on the year, between 15 and 40% over the winter figure. The rhythm of variation was between 18 and 24 months (Bartsch 2012).

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. Wada (2013) found that melatonin levels varied depending on sex and body size in a group of healthy preschool Japanese children. A study by Zarazaga (2009) showed that there were significant differences between melatonin concentrations in blood taken from the 2 jugular veins at the same time in the same individual sheep. The authors did not have an explanation for this phenomenon, but suggested it could have implications for experimental protocols.

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 (Kaur & Ling 2008, Reiter 2008). It is naturally synthesized from the amino acid tryptophan via synthesis of serotonin. Melatonin is also essential for glucose homoeostasis and regulation (Kedziora-Kornatowska 2009). Ximenes (2009) and Makay (2009) propose mechanisms by which melatonin's anti-oxidant properties may be explained.

The pineal gland, which produces a large proportion of the body's melatonin, is a sensor of inflammation mediators and plays a central role in the control of the inflammatory response (Fernandes 2009). Recent magnetic resonance imaging studies suggest that human plasma and saliva melatonin levels are partially determined by the pineal gland volume (Bumb 2014). Pineal volume appears to be reduced in patients with primary insomnia compared to healthy controls.

Melatonin has been detected in multiple extrapineal tissues including the brain, retina, lens, cochlea, Harderian gland, airway epithelium, skin, gastrointestinal tract, liver, kidney, thyroid, pancreas, thymus, spleen, immune system cells, carotid body, reproductive tract, and endothelial cells. Melatonin is also present in essentially all biological fluids including cerebrospinal fluid, saliva, bile, synovial fluid, amniotic fluid, and breast milk (Acuña-Castroviejo 2014).

Tan (2002) described how melatonin has the ability to repair damaged biomolecules. Unlike the classical antioxidants, melatonin is devoid of prooxidative activity and all known intermediates generated by the interaction of melatonin with reactive species are also free radical scavengers. This phenomenon is defined as the free radical scavenging cascade reaction of the melatonin family. Due to this cascade, one melatonin molecule has the potential to scavenge up to 4 or more reactive species. This makes melatonin very effective as an antioxidant. Under in vivo conditions, melatonin is often several times more potent than vitamin C and E in protecting tissues from oxidative injury.

Melatonin also synergizes with vitamin C, vitamin E and glutathione in the scavenging of free radicals. Melatonin has been detected in vegetables, fruits and a variety of herbs. In some plants,

especially in flowers and seeds (the reproductive organs which are most vulnerable to oxidative insults), melatonin concentrations are several orders of magnitude higher than measured in the blood of vertebrates. Melatonin in plants not only provides an alternative exogenous source of melatonin for herbivores but also suggests that melatonin may be an important antioxidant in plants which protects them from a hostile environment that includes extreme heat, cold and pollution, all of which generate free radicals (Tan 2000).

Melatonin has also been found in grape products, such as dessert wines and balsamic vinegars (Vitalini 2013).

Alterations in melatonin receptor expression as well as changes in endogenous melatonin production have been shown in circadian rhythm sleep disorders, Alzheimer's and Parkinson's diseases, glaucoma, depressive disorder, breast and prostate cancer, hepatoma and melanoma (Pandi-Perumal 2008b).

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 eyes, the bone marrow cells, gastrointestinal tract, skin, 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. Melatonin influences almost every cell and can be traced in membrane, cytoplasmic, mitochondrial and nuclear compartments of the cell.

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). In a study by Djeridane (2005) older rats produced less melatonin than younger ones, and they also produced less in periods of longer light exposure (summer) than times of equal exposure, suggesting that pineal melatonin levels are more sensitive to photoperiod changes in older, but not younger animals.

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.

A lack of melatonin has been identified as a potential factor in the development of breast cancer in female shift workers (Richter 2011). The peak production time of melatonin can be shifted by careful environmental manipulation to increase its production in night shift workers. Papantoniou (2014) found that night shift work affects levels and timing of melatonin production and may relate to future cancer risk. 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.

From a clinical point of view, provided that a person is not exposed to light at night, the daily profile of circulating melatonin provides a reliable estimate of the timing of the human suprachiasmatic nuclei (SCN) (the master clock in the hypothalamus).. Melatonin agonists have been developed for treating circadian, psychiatric and sleep disorders. These drugs may target the SCN for improving circadian timing or act indirectly at some downstream level of the circadian network to restore proper internal synchronization (Pevet & Challet 2011).

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). Ben-Moshe Livne (2016) found that the molecular clock in the melatonin-producing cells of the pineal gland plays a key role in modulating circadian rhythms of behaviour.

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 (Zeitzer 1999). Sanchez-Hidalgo (2009) reports age-related changes in melatonin synthesis in some rat peripheral organs. The authors suggest that the thymus may develop compensatory mechanisms to counteract the loss of immune activity and consequently, the loss of the potent antioxidant, during physiological ageing. Scientific research has not made consistent conclusions about changes in melatonin level with age. Bertrand (2010) found that the availability of gut 5-HT and melatonin is increased in aged mice and melatonin treatment suppresses natural gastrointestinal production of 5-HT and melatonin in the aged mouse intestine.

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.

Melatonin regulates the neuroimmuno-endocrine axis and is functionally important to the circadian rhythm, tumour suppression and immunity. In the CNS, melatonin exerts neuroprotective effects in many diseases, such as Parkinson's disease, Alzheimer's disease and ischaemic brain injury (Yu 2017).

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.

The regulatory function of melatonin on immune mechanisms is seasonally dependent. Melatonin-induced seasonal changes in immune function have been implicated in the pathogenesis of seasonal affective disorder and rheumatoid arthritis (Srinivasan 2008).

Age-related biological changes and increased life span

Ageing has been proposed as the major risk factor in most neurodegenerative disorders. Some studies (Akbulut 2008, Caballero 2008, 2009, Paredes 2009, García 2010 Ni 2013, Terán 2012, Mukda 2016), have concluded that exogenous melatonin had a potential role for retardation of age-related oxidative events. Tan (1999) found that even in young animals there is insufficient endogenously produced melatonin to detoxify hydroxyl radicals. The accumulated damage induced by the escaped HO. that results when the HO. avoids detoxification over the course of a life time may directly or indirectly accelerate aging and aging-related diseases.

Song (2016) found that melatonin exerted protection against aging-induced fertility decline and maintenance of mitochondrial redox balance.

Reiter (2008) found melatonin had the ability to reduce the severity of a variety of age-related diseases, including Alzheimer's disease, sleep disturbances in Parkinson's disease (Srinivasan 2011), amyotrophic lateral sclerosis (ALS) Huntington's disease, age-related macular degeneration (AMD) (Blasiak 2016), stroke and brain trauma (Pandi-Perumal 2013), that have as their basis free radical damage.

Ovarian aging is characterized by gradual declines in oocyte quantity and quality. Tamura (2017) found that melatonin delays ovarian aging in a number of ways including antioxidant action, maintaining telomeres, stimulating SIRT expression and ribosome function, and by reducing autophagy.

Melatonin was found to decrease the oxidative load accompanying ageing and it augmented general immunity (Vishwas 2013). Melatonin was administered to mice prone to aging. The aging process was counteracted by the supplementary melatonin, probably through its effect on mitochondrial physiology (Rodríguez 2008).

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 (Anisimov 2003, Rodriguez 2007). It restored some of the ageing effects in mice (Morioka 1999, Okatani 2002, 2003, Gutierrez-Cuesta 2008).

Cell survival was augmented and changes in biochemical parameters as a result of oxidative stress in ageing yeast cultures were ameliorated by the addition of melatonin (Owsiak 2010).

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).

Jonsson (2010) suggested that melatonin related genes might be interesting candidates for further investigation in the search for genes involved in autism spectrum disorders and related neurobehavioral conditions.

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).

Microwave radiation causes body mass decrease and anxiety related behaviour in rats, however melatonin causes a reverse of those effects on both body weight and behaviour of irradiated animals (Sokolovic 2012).

Bladder

Melatonin significantly improved bladder symptoms and histological damage in rats with induced cystitis (Zhang 2013).

Blood Brain barrier

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

Blood flow

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 protected the liver (Okatani 2003) testicles (Duru 2008) kidneys (Ersoz 2009) and the heart (Lochner 2013), from damage due to restricted, then restored, blood flow.

Melatonin and 1400W (Kesik 2009), or melatonin and s-methyl isothiourea (Tunc 2010) either alone or in combination, were efficient in ameliorating experimental ischemia reperfusion injury of the intestines.

Blood pressure

The chronic administration of melatonin to individuals with hypertension induces a measurable drop in night time systolic and diastolic blood pressure (Reiter 2009). Preventive treatment with melatonin helps to eliminate negative impacts of the earth's weather on patients with hypertensive disease (Rapoport & Breus 2011).

In an experiment on rats, melatonin not only prevented the increase in blood pressure during the developing stage of stress-induced hypertension (SIH), but it also reduced the blood pressure of rats that had already developed SIH (HL Li 2009).

Melatonin could be used as an additional treatment supporting hypotensive therapy in elderly primary essential hypertensive (EH) patients (Kedziora-Kornatowska 2008).

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. Ersahin (2009) found that melatonin alleviated the oxidative stress caused by haemorrhage, helped preserve blood-brain barrier permeability and reduced brain oedema.

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 (2008, 2010) also found that melatonin reduced hypoxic damage to the neonatal brain, due, they hypothesised to its antioxidant properties.

Burns

Melatonin protected against myocardial injury in severely-burned rats (Han & Xu 2012).

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. A review by Su (2017) highlights current advances in understanding the molecular mechanisms by which melatonin counteracts tumour metastases, including experimental and clinical observations. Melatonin's significant atoxic, apoptotic, oncostatic, angiogenetic, differentiating and antiproliferative properties against all solid and liquid tumours have been documented. Thanks, in fact, to its considerable functional versatility, it can exert both direct and indirect anticancer effects in factorial synergy with other differentiating, antiproliferative, immunomodulating and trophic molecules that form part of anticancer treatment (Di Bella 2013).

Melatonin decreased spontaneous tumour development in mammary and uterine neoplasms in rats kept in constant light (Vinogradova 2007). The same team of authors (Vinogradova 2008) found that nocturnal administration of melatonin with drinking water (10 mg/l) prevented the adverse effects of constant and natural lighting on homeostasis and inhibited spontaneous tumorigenesis, particularly, that in the hemopoietic system in male rats.

It is highly protective of oxidative damage to human blood cells (Vijayalaxmi 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.*" Melatonin (Othman [2008](#), Martín [2010](#)) and lycopene (the pigment in tomatoes) supplementation (Al-Malki [2012](#)) helped antioxidant defence against chemotherapy toxicity. Saxena ([2009](#)) found that melatonin reduced memory deficits and neuronal degeneration produced as side effects by anticancer chemical streptozotocin. Melatonin, as an adjuvant therapy, can be beneficial in treating patients suffering from breast cancer, hepatocellular carcinoma or melanoma (Moselhy & Al Mslmani [2008](#), Srinivasan [2011](#)), and in a meta-analysis by Dziegel ([2008](#)) melatonin had an antiproliferative effect on tumours as part of therapy.

Jang ([2009](#)) found that melatonin increased radiation-induced apoptosis in leukaemia cells, at the same time reducing apoptosis in normal cells in mice. A useful supplement to take during cancer radiation treatment. Melatonin was found to have anticancer effects in human myeloid cells (Bejarano [2009](#)). Administering melatonin in combination with other drugs in cancer treatment (Irinotecan (Kontek & Nowicka [2013](#)), can modulate their effectiveness, allowing for optimisation of treatment dosages, especially in aggressive triple negative breast cancer in African American women (Oprea-Ilies [2013](#)).

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](#), Schernhammer & Hankinson [2009](#), 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*".

Umit ([2012](#)) found that melatonin administration reduced the incidence, latency time and tumour volume of induced mammary cancers in rats.

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 xenooestrogens 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 (Schernhammer [2010](#)) and postmenopausal (Schernhammer [2008](#)) women's risk of developing breast cancer may be inversely related to overnight melatonin production.

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.

Melatonin directly targeted glioma tumour cells by altering glioblastoma stem-like cells' (GSCs) biology and inhibiting GSC proliferation (Zheng 2017) and glioma-initiating cells (Kinker 2016). GSCs display self-renewing and tumour-propagating capacity playing a particularly important role in maintaining tumour growth, therapeutic resistance, and tumour recurrence. Additionally, melatonin altered GSCs in such a way as to inhibit tumour initiation and propagation (Chen 2016).

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. Markt (2015) found significant gene-based associations with fatal prostate cancer and 6-sulfatoxymelatonin levels.

Melatonin was found to be a pro-apoptotic and pro-necrotic agent for pancreatic cancer cells. These effects were found both *in vitro* and *in vivo* (Xu 2013).

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 Mukherjee 2012). 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).

A study by Sato (2013) found that melatonin concentrations during sleep in obese subjects were significantly lower than those in non-obese subjects in the winter. They said that decreased nocturnal melatonin concentrations during winter in obese men may be related to higher heart rates, and this may suggest that obese men are at an increased risk of a cardiovascular incident during sleep, especially in the winter.

Melatonin is an important endogenous signal able to synchronise circadian oscillations in the cardiovascular system. It may be effective especially in situations when the circadian control is weakened or the organism must adapt to rapid changes in rhythmic environmental conditions (Zeman & Herichova 2013).

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. Rezzani (2009) found that melatonin reduced damage resulting from CsA cardiotoxicity.

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). Among products where melatonin has been identified include wine, olive oil, tomato, beer, and others (Favero 2017). Interestingly,

consumed melatonin in plant foods or melatonin supplementation may promote health benefits by virtue of its multiple properties and it may counteract pathological conditions also related to cardiovascular disorders, carcinogenesis, neurological diseases and aging.

It was suggested by Rezzani (2013) that melatonin treatment may help in the early stages of artherosclerosis (clogging of the arteries) due to its antioxidant properties.

Central Nervous System (CNS) injuries and diseases

Das (2008, 2010) found that melatonin may be an effective neuroprotective agent to attenuate motoneuron death, and reduce oxidative stress in CNS injuries and diseases.

Chemicals

Melatonin was found to significantly increase the benefits of treatments for paraquat toxicity (Gocgeldi 2008).

Dementia

People with Alzheimer's do not have normal melatonin levels. Dr Gordon Crawford (CPS Research, Glasgow) thought that slow release melatonin may reduce some of the symptoms, increasing quality of life in both patients and carers. They found that the study participants functioned better during the day, possibly due to a better quality sleep pattern. He said that the melatonin was remarkably safe and virtually free from side effects. Disrupted melatonin production in aging and in Alzheimer's disease (AD) are taking place as early as in the very first preclinical AD stages; light therapy and melatonin supplementation has shown promising positive results (Wu & Swaab 2005).

Melatonin helped reduce the severity of Alzheimer's disease (Rodriguez 2007, Masilamoni 2008, O'Neal-Moffitt 2015) and slowed its progression (Cheng 2006, Berra & Rizzo 2009, Olcese 2009), possibly by preventing mitochondrial membrane damage (Rosales-Corral 2012), neurodegenerative inflammation and altered proteosomal processing with abnormal activation of enzymes (Srinivasan 2010), modulation of apoptosis and protection of the cholinergic system (Feng 2004). 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.