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Melatonin antioxidative defense: therapeutical implications for aging and neurodegenerative processes.

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Abstract

The pineal product melatonin has remarkable antioxidant properties. It is secreted during darkness and plays a key role in various physiological responses including regulation of circadian rhythms, sleep homeostasis, retinal neuromodulation, and vasomotor responses. **It scavenges hydroxyl, carbonate, and various organic radicals as well as a number of reactive nitrogen species**. Melatonin also enhances the antioxidant potential of the cell by stimulating the synthesis of antioxidant enzymes including superoxide dismutase, glutathione peroxidase, and glutathione reductase, and by augmenting glutathione levels. **Melatonin preserves mitochondrial homeostasis, reduces free radical generation and protects mitochondrial ATP synthesis by stimulating Complexes I and IV activities**. The decline in melatonin production in aged individuals has been suggested as one of the primary contributing factors for the development of age-associated neurodegenerative diseases**. The efficacy of melatonin in preventing oxidative damage in either cultured neuronal cells or in the brains of animals treated with various neurotoxic agents, suggests that melatonin has a potential therapeutic value as a neuroprotective drug in treatment of Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), Huntington's disease (HD), stroke, and brain trauma. Therapeutic trials with melatonin indicate that it has a potential therapeutic value as a neuroprotective drug in treatment of AD, ALS, and HD.** In the case of other neurological conditions, like PD, the evidence is less compelling. Melatonin's efficacy in combating free radical damage in the brain suggests that it can be a valuable therapeutic agent in the treatment of cerebral edema following traumatic brain injury or stroke. Clinical trials employing melatonin doses in the range of 50-100 mg/day are warranted before its relative merits as a neuroprotective agent is definitively established.