

## Melatonin: A Multifunctional Indoleamine with Powerful Antioxidant Properties

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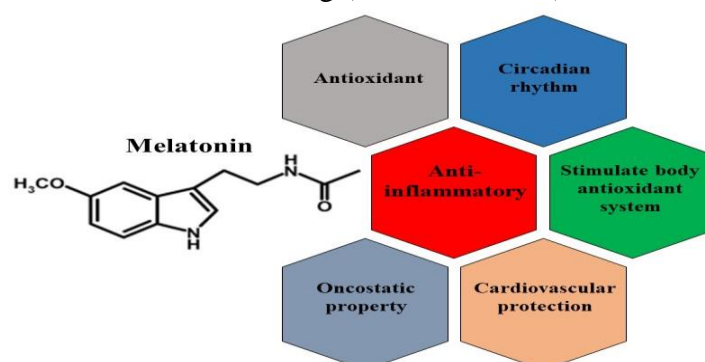
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### SUMMARY

Melatonin is a versatile indoleamine found in organisms from prokaryotes to eukaryotes. It plays a vital role in regulating circadian rhythms, acting as a hormone that synchronizes the body with day-night variations. Melatonin functions as a potent antioxidant, scavenging free radicals and producing metabolites with even stronger antioxidant properties. It stimulates the body's antioxidant enzymes and reduces oxidative stress. Melatonin's protective effects have been observed in conditions like ischemia-reperfusion injury during strokes and heart attacks. Additionally, it exhibits indirect anti-inflammatory actions by reducing reactive species. The intriguing evolutionary origins of melatonin suggest its initial role as an antioxidant, particularly in mitochondria and chloroplasts. Overall, melatonin's multifaceted functions make it a fascinating molecule with potential implications for health and disease prevention.

### INTRODUCTION

Melatonin was first discovered in the bovine pineal gland in the 1950s (Lerner et al., 1958). It derives its name from its ability to aggregate melanin molecules in melanocyte cells of amphibians and is derived from the neurotransmitter serotonin. Melatonin is found ubiquitously in every organism, from extinct and living prokaryotes to humans and plants, and it performs a wide range of functions including circadian rhythm regulation, antioxidant activity, anti-inflammation, and oncostatic properties (Tan et al., 2003). The biosynthesis of melatonin in vertebrates primarily occurs during nighttime and is regulated by light (Rajiv et al., 2016; Sanjita Devi et al., 2022). Its main function in vertebrates is hormone-like, helping to synchronize the body with the external environment and regulate circadian rhythms, earning it the nickname "dark hormone" due to its higher production levels during the night (Reiter, 1991). Various metabolic disorders, including cancer, type 2 diabetes, heart diseases, and stroke, have been closely linked to alterations in the biological clock and melatonin biosynthesis (Reiter et al., 2000). Melatonin is believed to have originated approximately 2.5 billion years ago, initially serving as an antioxidant before adopting additional functions throughout evolution (Tan et al., 2007). Although, melatonin is present ubiquitously within cells, its distribution is unequal, with higher concentrations found in mitochondria and chloroplasts (Tan et al., 2007). As mitochondria and chloroplasts play active roles in energy production, they generate substantial amounts of free radicals. Thus, the presence of a potent antioxidant like melatonin is crucial for their efficient functioning (Tan et al., 2007).



**Figure 1: The figure illustrates the diverse and multifunctional properties of melatonin.**

Mitochondria and chloroplasts are predicted to be the original sites of melatonin production within cells, with higher melatonin levels observed in plant cells that contain both organelles compared to animal cells (Tan et al., 2007). Melatonin surpasses well-known antioxidants such as ascorbic acid (Vitamin C), Trolox, tocopherols (Vitamin E), and glutathione in terms of potency and efficiency (Tan et al., 2007).

Melatonin functions as an antioxidant through several mechanisms, including direct scavenging of free radicals, upregulation of the cellular antioxidant system, and downregulation of prooxidant enzymes (Reiter et

al., 2001). While melatonin itself has a minor role in scavenging free radicals, the metabolites produced during the reaction of free radicals with melatonin molecules exhibit greater antioxidant properties (Reiter et al., 2001; Tan et al., 2007). These metabolites, generated in a cascade manner, include cyclic 3-hydroxymelatonin (C-3HOM), N1-acetyl-N2-formyl-5-methoxy-knuramine (AFMK), and N-acetyl-5-methoxy-knuramine (AMK) (Tan et al., 2007). These metabolites have antioxidant effects on their own, with C-3HOM and AMK exhibiting even stronger antioxidant properties than melatonin itself (Tan et al., 2007). Through this cascade mechanism, a single melatonin molecule can scavenge up to ten free radicals, making it more efficient than other antioxidants (Tan et al., 2007).

Melatonin also plays a role in stimulating the body's antioxidant enzymes, such as glutathione reductase and glutathione peroxidase, which contribute to the reduction of oxidative stress (Reiter et al., 2001). Additionally, it suppresses the pro-oxidative enzyme nitric oxide synthase (NOS), further aiding in the reduction of oxidative stress (Reiter et al., 2001).

Extensive research has focused on the protective effects of melatonin against oxidative damage in the heart and brain (Reiter et al., 2001). Circulating melatonin levels have shown a strong correlation with reduced oxidative damage caused by conditions such as ischemia-reperfusion injury during brain strokes and heart attacks (Reiter et al., 2001). Ischemia-reperfusion refers to the temporary deprivation of oxygenated blood followed by its reintroduction, leading to a surge in reactive oxygen species and reactive nitrogen species. These reactive species disrupt cellular functions and contribute to cell death (Reiter et al., 2001). Melatonin has demonstrated its ability to protect against such oxidative damage resulting from ischemia-reperfusion conditions (Reiter et al., 2001). Furthermore, melatonin exhibits indirect anti-inflammatory actions by reducing the levels of reactive species, as inflammation is often associated with the generation of free radicals (Reiter et al., 2001).

## CONCLUSIONS:

Melatonin is a multifaceted compound with diverse functions in various organisms. It plays a crucial role in regulating circadian rhythms, acting as an antioxidant, reducing inflammation, and displaying oncostatic properties. Mitochondria and chloroplasts are key sites of melatonin production, where its potent antioxidant properties help maintain cellular functions. Melatonin's ability to scavenge free radicals, stimulate antioxidant enzymes, and suppress pro-oxidative enzymes contributes to its protective effects against oxidative damage. Additionally, melatonin's role in reducing inflammation further enhances its overall beneficial effects. Understanding the diverse functions of melatonin provides valuable insights into its potential therapeutic applications in various health conditions (Reiter et al., 2001; Tan et al., 2007).

## REFERENCES:

- Lerner, A.B., Case, J.D., Takahashi, Y., Lee, T.H., Mori, W., 1958. Isolation of melatonin, the pineal gland factor that lightens melanocytes. *J. Am. Chem. Soc.* 80(10), 2587-2587.
- Rajiv, C., Sanjita Devi, H., Mondal, G., Devi, S.D., Khan, Z.A., Yumnamcha, T., Bharali, R., Chattoraj, A., 2016. Daily and Seasonal Expression Profile of Serum Melatonin and Its Biosynthesizing Enzyme Genes (*tph1*, *aanat1*, *aanat2*, and *hiomt*) in Pineal Organ and Retina: A Study under Natural Environmental Conditions in a Tropical Carp, *Catla catla*. *Journal of Experimental Zoology Part A: Ecological Genetics and Physiology* 325(10), 688-700.
- Reiter, R.J., 1991. Melatonin: The chemical expression of darkness. *Mol. Cell. Endocrinol.* 79(1), C153-C158.
- Sanjita Devi, H., Rajiv, C., Mondal, G., Khan, Z.A., Devi, S.D., Bharali, R., Chattoraj, A., 2022. Influence of photoperiod variations on the mRNA expression pattern of melatonin bio-synthesizing enzyme genes in the pineal organ and retina: A study in relation to the serum melatonin profile in the tropical carp *Catla catla*. *J. Fish Biol.* 101(6), 1569-1581.
- Tan, D.-X., Manchester, L.C., Hardeland, R., Lopez-Burillo, S., Mayo, J.C., Sainz, R.M., Reiter, R.J., 2003. Melatonin: a hormone, a tissue factor, an autocoid, a paracoid, and an antioxidant vitamin. *J. Pineal Res.* 34(1), 75-78.