

# Unveiling the Protective Role of Melatonin in Osteosarcoma

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## Description

Osteosarcoma is a rare yet aggressive form of bone cancer that primarily affects children and young adults. Despite advancements in treatment modalities, including surgery, chemotherapy, and radiation therapy, the prognosis for osteosarcoma patients remains challenging. Therefore, there is a pressing need to explore alternative therapeutic strategies that can enhance treatment outcomes and improve patient survival rates. In recent years, melatonin, a hormone primarily synthesized by the pineal gland, has emerged as a promising candidate for adjunctive therapy in osteosarcoma management. This article aims to elucidate the protective role of melatonin in osteosarcoma and its potential implications for clinical practice [1,2].

Melatonin, often referred to as the "hormone of darkness," plays a crucial role in regulating the sleep-wake cycle and circadian rhythms. However, its functions extend beyond sleep regulation, as melatonin exhibits potent antioxidant, anti-inflammatory, and oncostatic properties. Melatonin is synthesized and released in response to darkness, with levels peaking during the night and declining during daylight hours. In addition to its endogenous production, melatonin can also be obtained through dietary sources and supplements. Osteosarcoma arises from primitive bone-forming mesenchymal cells and is characterized by the proliferation of malignant osteoblasts. The exact etiology of osteosarcoma remains unclear, although several risk factors, including genetic predisposition, exposure to ionizing radiation, and certain hereditary conditions, have been implicated in its development. The hallmark of osteosarcoma is the production of osteoid matrix by malignant cells, leading to the formation of osteolytic lesions within the bone tissue. Metastasis, particularly to the lungs, is a frequent complication in advanced osteosarcoma cases and is associated with poor prognosis [3].

Melatonin exerts potent antioxidant effects by scavenging free radicals and reducing oxidative stress-induced damage. Osteosarcoma cells are characterized by increased oxidative stress, which contributes to tumor progression and resistance to therapy. Melatonin's antioxidant properties help mitigate oxidative damage, thereby inhibiting tumor growth and enhancing the efficacy of conventional treatments such as chemotherapy and radiotherapy. Chronic inflammation plays a crucial role in the development and progression of various cancers, including osteosarcoma. Melatonin exhibits anti-inflammatory properties by modulating the activity of pro-inflammatory cytokines and inhibiting the nuclear Factor-Kappa B (NF- $\kappa$ B) signaling pathway. By attenuating inflammation within the tumor microenvironment, melatonin suppresses osteosarcoma cell proliferation, invasion, and metastasis. The immune system plays a pivotal role in tumor surveillance and eradication. However, osteosarcoma cells can evade immune detection and suppress antitumor immune responses. Melatonin enhances immune function by promoting the activity of Natural Killer (NK) cells, cytotoxic T lymphocytes, and dendritic cells, thereby bolstering the host's immune defenses against osteosarcoma [4].

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**Anti-proliferative and Pro-apoptotic Actions:** Melatonin inhibits osteosarcoma cell proliferation by inducing cell cycle arrest and apoptosis. It modulates various signaling pathways involved in cell growth and survival, including the PI3K/Akt/mTOR pathway and the p53 tumor suppressor pathway. By promoting apoptosis and inhibiting aberrant cell proliferation, melatonin impedes tumor progression and sensitizes osteosarcoma cells to chemotherapy-induced cell death. The preclinical evidence supporting the protective role of melatonin in osteosarcoma is compelling, highlighting its potential as an adjuvant therapeutic agent in combination with conventional treatments. Clinical trials evaluating the efficacy and safety of melatonin supplementation in osteosarcoma patients are warranted to validate its therapeutic benefits and optimize treatment protocols. Additionally, further research is needed to elucidate the optimal dosage, timing, and duration of melatonin therapy, as well as its potential interactions with other medications [5].

Melatonin represents a promising adjunctive therapy for osteosarcoma, offering multifaceted protective effects against tumor growth, metastasis, and treatment resistance. By targeting key pathways involved in cancer pathogenesis, including oxidative stress, inflammation, and immune evasion, melatonin holds great potential for improving treatment outcomes and enhancing the quality of life for osteosarcoma patients. Continued research efforts are essential to translate the preclinical findings into clinical practice and establish melatonin as a standard therapeutic option in the management of osteosarcoma.

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## Conflict of Interest

None.

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