Therapeutic actions of melatonin in cancer: possible mechanisms.

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Source
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Abstract
Melatonin is a phylogenetically well-preserved molecule with diverse physiological functions. In addition to its well-known regulatory control of the sleep/wake cycle, as well as circadian rhythms generally, melatonin is involved in immunomodulation, hematopoiesis, and antioxidative processes. Recent human and animal studies have now shown that melatonin also has important oncostatic properties. Both at physiological and pharmacological doses melatonin exerts growth inhibitory effects on breast cancer cell lines. In hepatomas, through its activation of MT1 and MT2 receptors, melatonin inhibits linoleic acid uptake, thereby preventing the formation of the mitogenic metabolite 1,3-hydroxyoctadecadienoic acid. In animal model studies, melatonin has been shown to have preventative action against nitrosodiethylamine (NDEA)-induced liver cancer. Melatonin also inhibits the growth of prostate tumors via activation of MT1 receptors thereby inducing translocation of the androgen receptor to the cytoplasm and inhibition of the effect of endogenous androgens. There is abundant evidence indicating that melatonin is involved in preventing tumor initiation, promotion, and progression. The anticarcinogenic effect of melatonin on neoplastic cells relies on its antioxidant, immunostimulating, and apoptotic properties. Melatonin's oncostatic actions include the direct augmentation of natural killer (NK) cell activity, which increases immunosurveillance, as well as the stimulation of cytokine production, for example, of interleukin (IL)-2, IL-
6, IL-12, and interferon (IFN)-gamma. 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. The increased incidence of breast cancer and colorectal cancer seen in nurses and other night shift workers suggests a possible link between diminished secretion of melatonin and increased exposure to light during nighttime. The physiological surge of melatonin at night is thus considered a "natural restraint" on tumor initiation, promotion, and progression.

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