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1017 – Melatonin oncostatic mechanisms as an adjuvant strategy: a synthesis of molecular evidence

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Introduction: Melatonin (N-acetyl-5-methoxytryptamine) has transcended its classic role as a circadian regulator to emerge as a potent oncostatic agent. Despite its pleiotropic effects, its integration into clinical mastology remains limited.

Objective: To synthesize molecular evidence on the role of melatonin in breast cancer progression and to analyze its potential therapeutic synergy.

Methodology: An integrative review was conducted through PubMed, SciELO and Cochrane databases, covering studies published between 2021 and 2024. The descriptors used were “Breast Neoplasms”, “Melatonin”, “Aromatase Inhibitors” and “Angiogenesis Inhibitors”. Eligibility criteria focused on mechanistic studies and clinical adjuvant therapy.

Results and Discussion: Melatonin exhibits a quadruple oncostatic mechanism: 1) Mitochondrial reprogramming: reverses the Warburg effect by inhibiting HIF-1 α and disinhibiting the pyruvate dehydrogenase complex (PDH), shifting metabolism toward oxidative phosphorylation; 2) Endocrine modulation: acts as a selective estrogen enzyme modulator (SEEM), negatively regulating aromatase promoters I.3 and II via the COX-2/PGE2 pathway, leading to a significant reduction in local estradiol synthesis; 3) Antiangiogenesis: suppresses VEGF and Angiopoietin-2, neutralizing the pro-angiogenic rebound frequently triggered by taxanes and vinca alkaloids; 4) Metastatic inhibition: upregulates E-cadherin and inhibits MMP-9, suppressing the epithelial-mesenchymal transition (EMT). Data indicate that 1 nM melatonin can increase radiosensitivity by up to 75% in ER+ models and provide neuroprotection against chemotherapy-induced cognitive impairment.

Conclusion: Melatonin acts as a mitochondrial and epigenetic modulator, reprogramming tumor metabolism and inhibiting angiogenesis. Due to its low toxicity and favorable cost-benefit ratio, it stands out as a potential adjuvant therapy in breast cancer, reinforcing the need for clinical trials to improve outcomes and the quality of life of patients.

Ethics: Public data.

Keywords: breast neoplasms; melatonin; aromatase inhibitors; angiogenesis inhibitors.