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Commentary

Sleep, tryptophan metabolism, and breast cancer: Implications for public health nutrition

Nádia Raci Marques Pereira[1], **Isabela Antunes Ishikura**[1,2], **Sergio Tufik**[1,2], **Helena Hachul**[1,2,*]

[1]Department of Psychobiology, Universidade Federal de São Paulo (UNIFESP), São Paulo, Brazil; [2]Sleep Institute, Associação Fundo de Incentivo à Pesquisa (AFIP), São Paulo, Brazil

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***Corresponding Author**
Hachul H
helenahachul@gmail.com
PHONE: +55 11 2149-0160
ORCID: 0000-0002-3661-582X

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Highlights/Key Messages

- Sleep disturbance is highly prevalent in women with breast cancer.
- Tryptophan metabolism links sleep regulation and cancer biology.
- L-kynurenine is the primary breakdown product (metabolite) of L-tryptophan
- Personalized nutrition may support sleep health in breast cancer.
- Clinical studies are needed before therapeutic recommendations involving tryptophan can be made.

Abstract

Breast cancer remains the most frequently diagnosed cancer among women worldwide and represents a major public health challenge. Sleep disturbances are highly prevalent in women with breast cancer and have been associated with impaired quality of life, circadian disruption, immune dysregulation, and adverse clinical outcomes. Tryptophan metabolism has emerged as a potential biological link between sleep regulation and breast cancer through its roles in serotonin and melatonin synthesis and the kynurenine pathway, which is implicated in tumor progression and immune modulation. This commentary discusses current evidence on the complex and context-dependent role of tryptophan metabolism, highlighting its relevance to sleep health, cancer biology, and discusses nutritional strategies from a public health perspective. While adequate dietary tryptophan may contribute to sleep regulation and well-being, excessive activation of tryptophan catabolism through the kynurenine pathway may promote an immunosuppressive tumor microenvironment. Therefore, current evidence does not support tryptophan supplementation in women with active breast cancer. Further clinical and translational studies are needed to clarify the therapeutic potential and safety of targeting tryptophan metabolism in breast cancer care.

Introduction

Breast cancer remains the most frequently diagnosed cancer among women worldwide and represents a major public health challenge due to its substantial impact on morbidity, quality of life, and healthcare systems (Bray et al., 2024). While considerable attention has been directed toward biological and genetic determinants, modifiable behavioral and nutritional factors that may influence both disease outcomes and survivorship remain comparatively underexplored (Bray et al., 2024; Carson et al., 2025).

Among these factors, sleep health and nutrition have emerged as important yet often underrecognized determinants of well-being in women with breast cancer (Carson et al., 2025; Zhang et al., 2025).

In this context, emerging evidence suggests that tryptophan metabolism represents a key interface linking sleep regulation and breast cancer outcomes, integrating circadian, metabolic, and immune pathways (Cui et al., 2025; Liu et al., 2025; Li et al., 2023).

Tryptophan plays a central role in sleep physiology as a precursor of serotonin and melatonin, and dietary intake has been associated with improved sleep quality (Mei et al., 2025). Beyond its established role in sleep regulation, tryptophan metabolism has also emerged as an important pathway in cancer biology, particularly through activation of the kynurenine pathway, which contributes to tumor progression and immune evasion (Cui et al., 2025). Clinical evidence further supports this concept. In a study of 79 breast cancer survivors, approximately 19% exhibited a high psychoneurological symptom burden,

Keywords: breast cancer; sleep; tryptophan metabolism; kynurenine pathway; melatonin; public health nutrition.

including sleep disturbance. These patients had significantly lower circulating tryptophan levels than those with a lower sleep symptom burden (227.5 vs. 283.9 arbitrary units). A higher kynurenine-to-tryptophan ratio was independently associated with greater symptom burden (Li et al., 2023). This dual role highlights the context-dependent effects of tryptophan, reflecting a complex metabolic balance.

Sleep disturbances are highly prevalent in women with breast cancer and are increasingly recognized as a modifiable factor associated with disease progression. A recent systematic review reported that sleep disturbances affect approximately 60% of patients undergoing breast cancer treatment, underscoring the need for effective strategies to improve sleep in this population (Carson et al., 2025). Circadian disruption, reduced melatonin secretion, and poor sleep quality have been linked to immune dysregulation, hormonal imbalance, and inflammation (Zhang et al., 2025). These findings further support the biological relevance of tryptophan metabolism to the interplay between nutritional factors, sleep regulation, and tumor biology, given its involvement in both melatonin synthesis and oncogenic metabolic pathways (Cui et al., 2025).

Melatonin, derived from tryptophan, has demonstrated oncostatic and anti-proliferative effects in breast cancer through multiple molecular pathways (Hill et al., 2015). More recent evidence from a systematic review further supports these findings, highlighting the role of melatonin in inhibiting breast cancer progression through multiple molecular mechanisms (Alves et al., 2026). This raises the possibility that optimizing tryptophan availability within a balanced metabolic context may support circadian regulation and influence cancer-related outcomes. However, this concept requires careful evaluation, given that increased tryptophan metabolism via alternative pathways may also favor tumor progression (Cui et al., 2025; Ebokaiwe et al., 2025; Giatromanolaki et al., 2025; Wang et al., 2026).

Activation of tryptophan catabolism through enzymes such as indoleamine 2,3-dioxygenase 1 (IDO1) and tryptophan 2,3-dioxygenase (TDO2) has been associated with increased kynurenine production and modulation of the tumor immune microenvironment (Ebokaiwe et al., 2025; Wang et al., 2026; Giatromanolaki et al., 2025). This process contributes to reduced T-cell activity, impaired immune surveillance, and alterations in immune cell infiltration, supporting tumor progression. Moreover, shifts in downstream kynurenine metabolites may further shape tumor behavior and immune response, underlying the complexity of tryptophan metabolism in cancer. Recent evidence has expanded the understanding of tryptophan metabolism by emphasizing the roles of free tryptophan and the indole pathway, in addition to the kynurenine pathway, in regulating immune homeostasis and host responses relevant to cancer biology (Holeček, 2026).

In addition to its immunological effects, tryptophan metabolism may also influence tumor behavior through broader metabolic and microenvironmental interactions. The kynurenine pathway has been associated with changes in cellular metabolism, redox balance, and signaling pathways that support tumor adaptation and survival. Together, these findings indicate that tryptophan metabolism may influence tumor–host interactions through multiple interconnected biological pathways (Liu et al., 2025).

Recent evidence further supports the relevance of tryptophan metabolism as a dynamic and context-dependent system in cancer biology, involving interactions between tumor cells, immune responses, and metabolic pathways (Liu et al., 2025). In addition, alterations in tryptophan availability and its subsequent metabolites have been associated with psychoneurological symptoms commonly observed in patients with breast cancer, including sleep disturbances, fatigue, and mood alterations (Li et al., 2023). This broader perspective links tryptophan metabolism not only to tumor biology but also to symptom burden and patient well-being.

Taken together, these observations suggest that dietary tryptophan should be further investigated not only as a nutritional factor but also as a potential component of broader strategies to promote sleep health among women affected by breast cancer.

Current evidence supports a conceptual framework in which dietary tryptophan availability influences serotonin and melatonin synthesis, thereby contributing to circadian regulation and sleep health, while alterations in tryptophan catabolism through the kynurenine pathway may influence immune regulation and breast cancer progression (Claustrat & Gronfier, 2026; Liu et al., 2025; Hill et al., 2015). Recent evidence further supports this perspective, as a nutritional intervention rich in foods high in tryptophan was associated with increased sleep duration and reduced nocturnal wakefulness during breast cancer treatment (Van Keulen et al., 2026).

From a public health nutrition perspective, understanding the interactions between tryptophan metabolism, sleep regulation, and cancer biology may contribute to the development of integrative and personalized approaches aimed at improving quality of life and long-term survivorship. These approaches may include nutritional, circadian, and immunometabolic strategies tailored to individual metabolic and clinical characteristics.

Future research should evaluate multimodal interventions integrating nutritional counseling, dietary modulation of tryptophan intake, sleep optimization, and circadian health strategies to determine whether these approaches improve sleep quality, quality of life, and long-term survivorship in women with breast cancer. Additionally, individual variability in metabolism and dietary patterns should be considered, reinforcing the need for personalized approaches.

Author Contributions

NRMP: Conceptualization, Investigation, Methodology, Formal analysis, Writing – original draft, Writing – review & editing; IAI: Conceptualization, Data analysis, Writing – review & editing; ST: Conceptualization, Supervision, Writing – review & editing; HH: Conceptualization, Supervision, Project administration, Writing – review & editing. All authors have read and approved the final version of the paper and its submission and have given consent for publication.

Declaration of Generative AI and AI-Assisted Technologies in Scientific Writing

The authors used ChatGPT (OpenAI) solely to assist with English language editing, grammar improvement, and enhancement of the clarity and readability of the manuscript. Artificial intelligence was not used to generate scientific content, analyze data, interpret results, or draw conclusions. All scientific content, interpretations, and final decisions remain the sole responsibility of the authors, who carefully reviewed and approved the final manuscript.

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Data Availability Statement

All relevant data are available within the manuscript

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Conflict of Interest

The authors report no conflicts of interest to disclose. All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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