REVIEWER'S REPORT

Manuscript No.: IJAR-55953

Title: *Mechanistic Study of Melatonin: A Systematic Review*

Recommendation:

Accept as it is ....

✓ Accept after minor revision.................

Accept after major revision ....

Do not accept (*Reasons below*) ....

Rating	Excel.	Good	Fair	Poor
Originality		✓		
Techn. Quality		✓		
Clarity		✓		
Significance	✓			

Reviewer Name: Dr S. K. Nath   **Date:** 28.01.26

Detailed Reviewer's Report

Strengths of the Study

- The manuscript provides a comprehensive and systematic overview of the molecular and cellular mechanisms by which melatonin exerts its physiological and therapeutic effects.
- The study adheres to PRISMA guidelines, indicating a rigorous and transparent review process.
- The inclusion of multiple databases (PubMed, Scopus, Web of Science, Google Scholar) enhances the breadth of literature coverage.
- The review covers a broad spectrum of melatonin's roles, including its antioxidant, anti-inflammatory, immune-regulatory, neuroprotective, and anticancer properties.
- The discussion integrates mechanistic insights with clinical relevance, offering valuable translational perspectives.

Weaknesses of the Study

- No explicit mention of whether the systematic review protocol was registered in a database such as PROSPERO, which could raise concerns about potential bias or protocol adherence.
- Lack of detailed inclusion/exclusion criteria, such as specific study designs (e.g., randomized controlled trials, in vivo, in vitro), which may affect reproducibility.
- The review encompasses a wide range of topics; however, it lacks a critical appraisal of the quality and risk of bias of the included studies.
- No mention of data extraction or synthesis methods beyond qualitative categorization, limiting the rigor of the evidence synthesis.
- Limited discussion on heterogeneity among studies or meta-analytic techniques for quantitative assessment.
- Presentational issues include some repetitive information and occasional lack of clarity in technical descriptions.
- The references list includes some studies from the early 1990s; more recent and high-impact evidence might have strengthened the review, especially in rapidly evolving fields like oncology and immunology.

Reviewer Comments

- **Title and Abstract Clarity** The title accurately reflects the content, emphasizing the mechanistic focus of the review. The abstract is clear, well-structured, and provides a succinct overview of background, objectives, methodology, main findings, and conclusion.

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- **Introduction and Objectives** The introduction effectively contextualizes melatonin's roles beyond sleep regulation, setting a comprehensive background. However, explicit research questions or objectives are not clearly stated, which would improve clarity and focus of the review.

- **Methodology and Statistical Analysis** While the methodology mentions adherence to PRISMA and database searches, it lacks detail about study selection criteria, quality assessment, and data extraction protocols. No formal meta-analyses or statistical evaluations are described or performed. Clarification on these points is necessary for assessing the robustness of the review.

- **Results and Discussion** The synthesis of mechanistic pathways is insightful but remains at a descriptive level. Incorporating critical analysis of study quality, comparing conflicting findings, and discussing limitations would improve scientific rigor. The discussion covers a broad range of effects but sometimes lacks depth regarding underlying molecular interactions.

- **Conclusion and Implications** The conclusion appropriately highlights melatonin's multifaceted roles and future research directions. However, concrete recommendations for clinical translation or specific areas needing further mechanistic elucidation are limited.

- **Ethical Clearance** As a systematic review, formal ethical approval is generally not required. The manuscript does not mention any need for ethical clearance, which is acceptable. No conflicts of interest or ethical concerns are evident.

- **Grammar, English Language, and Typographical Errors** Language is generally clear, though some sentences could benefit from improved clarity and conciseness. Minor typographical issues are minimal but should be reviewed for consistency.

- **Tables, Figures, Formatting, and References** The manuscript appears text-heavy, with no visible tables or figures, which could enhance clarity and data presentation. References are comprehensive but somewhat dated; integrating more recent studies would strengthen the manuscript.

Additional Note: Based on the review of the content provided and standard practices for scholarly publications, there are no indications or evidence within the text suggesting that this particular study has been previously published on the internet or elsewhere. To conclusively verify whether this work has been previously published, a dedicated plagiarism check or database search (e.g., PubMed, Google Scholar, or institutional repositories) would be necessary.