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REVIEWER'S REPORT

Manuscript No.: **IJAR-55953**

Title: Mechanistic Study of Melatonin: A Systematic Review

Recommendation:

Accept after major revision

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

Reviewer Name: Dr. Sudheer Aluru

Detailed Reviewer's Report

The manuscript presents a timely and comprehensive overview of melatonin's diverse mechanisms. The topic is suitable for the journal, and the authors have attempted a systematic approach. However, the manuscript in its current form reads more like a narrative or integrative review than a rigorous systematic review. Significant methodological and structural revisions are required before it can be considered for publication.

Major Comments

1. The authors claim adherence to PRISMA, but essential elements are missing: no PRISMA flow diagram, no number of records retrieved/screened/included, no risk-of-bias assessment, no study-type stratification, and no table summarizing included studies. Without these, the review does not meet methodological expectations for a systematic review and currently reads closer to a narrative review.
2. The "Results and Discussion" section presents a synthesized narrative of melatonin's functions without separating the factual findings of the reviewed studies (Results) from their interpretation and contextualization (Discussion). This conflation weakens the review's objectivity. The "Results" should systematically present the evidence from included studies (e.g., by pathway or

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system), while the "Discussion" should interpret these findings, discuss contradictions, and highlight gaps.

3. The oncology subsection would benefit from clearer differentiation between preclinical synergy with chemotherapy and clinical trial evidence.
4. Clinical applications are discussed appropriately, but safety, dosing variability, circadian timing, pharmacokinetics, and regulatory status across indications are insufficiently covered for a review claiming clinical relevance.
5. The "Future Perspectives" section is brief and could be expanded to include biomarker-guided use, chronotherapy strategies, combination therapies, and unresolved controversies.

Minor Comments

6. The "Methods" and "Results" in the abstract are too vague. Specify the number of studies included and summarize key mechanistic categories identified, not just broad physiological roles.
7. The "Data Analysis" section is unnecessary as a separate heading; its content should be integrated into the "Materials and Methods."
8. Minor language polishing is needed to reduce repetition and tighten phrasing in the Results/Discussion.