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REVIEWER'S REPORT

Manuscript No.: **IJAR-53414** Date: 20-08-2025

Title: Brassinosteroids a inter kingdom signaling molecules modulating sterioidogenesis in Polycystic Ovary Syndrome an In Silico study

Recommendation:
Accept as it is .....YES.....
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 Aamina

Reviewer's Comment for Publication.

The manuscript titled **"Brassinosteroids: Inter-Kingdom Signaling Molecules Modulating Steroidogenesis in Polycystic Ovary Syndrome – An In Silico Study"** explores the novel concept of plant-derived brassinosteroids as modulators of ovarian steroidogenesis in the context of polycystic ovary syndrome (PCOS). The work integrates endocrinology, phytochemistry, and computational biology, positioning brassinosteroids as potential therapeutic agents with relevance to metabolic and reproductive disorders.

The **abstract** presents the study's rationale clearly by highlighting the role of cholesterol availability, 17β-hydroxysteroid dehydrogenases, and aromatase as regulatory checkpoints in ovarian steroidogenesis. It emphasizes the structural similarities between brassinosteroids and oxysterols and notes the known pharmacological properties of brassinosteroids such as antihyperglycemic and anticholesterolemic effects. The study employs **in silico docking** and ADMET evaluation to assess interactions with key targets including aromatase, 17β-hydroxysteroid dehydrogenase, androgen receptor, and estrogen receptor, reporting higher docking scores compared to standard ligands. The abstract concludes with the potential of dietary brassinosteroids to downregulate ovarian steroidogenesis in PCOS, setting a strong foundation for further investigation.

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The introduction effectively contextualizes PCOS as a multifactorial endocrine disorder affecting 8–20% of women of reproductive age. It provides historical background beginning with Stein and Leventhal's 1935 description and progresses to the Rotterdam criteria (2013) and international evidence-based guidelines (2018). The discussion of PCOS symptomatology—hyperandrogenism, anovulation, cystic ovarian morphology, and associated metabolic dysfunctions such as insulin resistance, glucose intolerance, obesity, and cardiovascular risk—underscores the clinical burden of the disorder. The introduction successfully establishes the relevance of exploring alternative therapeutic pathways, including plant-derived compounds like brassinosteroids.

The manuscript's strength lies in its interdisciplinary approach, bridging plant hormone signaling with human endocrine regulation. By focusing on in silico docking studies using AutoDock 4.0 and ADMET predictions via SwissADME, the study demonstrates the potential pharmacological applicability of brassinosteroids beyond their plant physiological roles. The choice of targets—aromatase, 17β-hydroxysteroid dehydrogenase, androgen receptor, and estrogen receptor—is well justified in the context of PCOS pathophysiology.

Overall, the manuscript presents a novel and conceptually significant contribution to the understanding of inter-kingdom signaling and its translational potential in managing PCOS. It offers a unique perspective by suggesting dietary brassinosteroids as modulators of ovarian steroidogenesis, thus opening an intriguing avenue for future experimental and clinical research.