Journal of Chemistry Insights and Discoveries
Publisher: BioLuster Research Center Ltd.
Journal Home Page: Journal of Chemistry Insights and Discoveries
Journal DOI: https://doi.org/10.71193/jcid

Review Report

Final Title: Molecular Mechanisms of Genistein in Breast Cancer: From Oxidative Stress to Oncogenic Pathway Inhibition
Submission Title: Molecular Mechanisms of Genistein in Breast Cancer: From Oxidative Stress to Oncogenic Pathway Inhibition
Submission Date: June 08, 2025
Initial Editorial Assessment: July 01, 2025
Sent for Review: July 07, 2025
Review Completed: August 11, 2025
Accepted: August 24, 2025

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Round 1

Reviewer 1
Name: Jannatul Ferdous
Conflict of Interest: None
Date of Reviewer's Comments: May 25, 2025
Date of Author Response: July 15, 2025

Reviewer 1 Comments	Author Response
Reviewer Recommendation: Your review mentions several clinical studies with mixed outcomes. Could the authors clarify whether genistein is more beneficial in specific subtypes of breast cancer (e.g., ER-positive vs. triple-negative)? Is the risk-benefit profile population-dependent?	Thank you for your comment. GT is more beneficial potential benefits in both ER-positive and triple-negative subtypes. Yes, the risk-benefit profile is population-dependent.
What are the most pressing gaps in genistein research? Should future work prioritize pharmacokinetics, formulation improvement, or clinical validation?	Thank you for your comment. The most significant gaps in genistein research are well-designed clinical validation assessing genistein's efficacy and safety as a breast cancer therapeutic or preventive agent, low water solubility, and limited blood-brain barrier (BBB) penetration. Future research should prioritize clinical validation and formulation improvement.
Several pathways (PI3K/Akt, MAPK, Notch, etc.) are mentioned, but mechanistic connections are sometimes superficial. Could the authors create a more structured figure or table outlining which effects (e.g., apoptosis, cell cycle arrest) are linked to which signaling cascades?	Thank you for your valuable suggestion. We have included it in the result section of our manuscript.
The ADME profile suggests poor BBB permeability and low water solubility. How do these characteristics limit the potential for genistein in metastatic breast cancer, especially involving the brain?	Thank you for your comment. To overcome genistein's poor BBB permeability and low water solubility in metastatic breast cancer treatment, strategies such as nanoformulations, liposomal delivery systems, or prodrug approaches can be employed and we included this in our revised manuscript as future direction.
The review tends to emphasize genistein's benefits. Would the authors consider expanding the limitations or unresolved controversies surrounding its use?	Thank you for your comment. We have fixed it.
Some references lack DOI links. Adding these would improve accessibility.	Thank you. We have added all the DOI links.
The conclusion broadly advocates for genistein as a therapeutic agent but also acknowledges contradictions. Could this section be refined to provide clearer take-home messages?	Thank you for your suggestion. We have fixed it.
The manuscript contains grammatical issues (e.g., verb agreement, tense confusion). Do the authors plan to submit this for professional language editing before final submission?	Thank you for your feedback. We have tried our best to professional language editing before final submission.

Round 2

Reviewer 1 Name: Jannatul Ferdous Conflict of Interest: None Date of Reviewer's Comments: July 15, 2025 Date of Author Response: N/A	
Reviewer 1 Comments	**Author Response**
Reviewer Recommendation: Not responded	N/A

DOI: https://doi.org/10.71193/jcid.20250006 | Journal of Chemistry Insights and Discoveries | 01(01): 20250006