

Review Form 3

Journal Name:	Journal of Advances in Medicine and Medical Research
Manuscript Number:	Ms_JAMMR_130682
Title of the Manuscript:	The Hormonal Nexus of Lipedema and Gynecological Conditions: Therapeutic Insights with Gestrinone and Drospirenone
Type of the Article	Minireview Article

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This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound. To know the complete guidelines for the Peer Review process, reviewers are requested to visit this link:

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PART 1: Comments

	Reviewer's comment	Author's Feedback <i>(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)</i>
Please write a few sentences regarding the importance of this manuscript for the scientific community. A minimum of 3-4 sentences may be required for this part.	This manuscript sheds light on an underexplored and often ignored area by connecting hormonal imbalances in lipedema with gynecological conditions such as endometriosis and adenomyosis. Its emphasis on estradiol receptor dysregulation (ER $\alpha$ > ER $\beta$ ) and the therapeutic potential of progestins (like gestrinone and drospirenone) offers important insights for clinical management. By discussing shared hormonal pathways, the article opens more avenues for interdisciplinary research in endocrinology, gynecology, and adipose tissue disorders. Moreover, the proposal of targeted hormonal therapies may lead to significant improve in patient outcomes, though the clinical implications remain only hypothetical without further studies.	Thanks for the comments
Is the title of the article suitable? (If not please suggest an alternative title)	The title, "The Hormonal Nexus of Lipedema and Gynecological Conditions: Therapeutic Insights with Gestrinone and Drospirenone," is clear and captures the study's focus. However, it is slightly complex and could benefit from being simpler while retaining its specificity. Suggestion: "Hormonal Links Between Lipedema and Gynecological Disorders: Therapeutic Roles of Gestrinone and Drospirenone."	Thanks for the comments Noted and incorporated

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Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.	<p>The abstract is comprehensive, presenting the study's aim, methods, findings, and conclusion. However, it could be improved as follows:</p> <ul style="list-style-type: none"><li><u>Redundancy</u>: The phrase "addressing key hormonal imbalances" is repeated in different forms (e.g., "By addressing key hormonal imbalances, these medications represent promising strategies..." and "addressing physical and psychological pain, edema, and swelling"). Simplify for better clarity. (commented on in the review article)</li><li><u>Framing of the Abstract</u>: Mention the shared hormonal mechanisms with gynecological conditions earlier for better framing.</li><li><u>Limitations</u>: The abstract omits the study's limitations, which should be included to provide a balanced summary. For example, the reliance on narrative review methods limits the scope of the conclusions.</li><li><u>Future Of Study</u>: "Further research is needed to validate these findings through clinical trials and experimental models."</li></ul>	Noted and corrected
Is the manuscript scientifically, correct? Please write here.	<p>In general, the manuscript is scientifically accurate but presents a few ideas and statements that must be reconsidered:</p> <ul style="list-style-type: none"><li><b>Overgeneralization</b>: The statement that "...these medications represent promising strategies for managing lipedema" (Section: Conclusion) is not fully substantiated, as the evidence provided relies heavily on theoretical mechanisms and indirect data rather than clinical trials.</li><li><b>Study Design Limitations</b>: The reliance on a narrative review method (Section: Methods) lacks the robust nature of systematic reviews or meta-analyses, reducing the strength of the conclusions. This could be addressed by including a broader and more structured analysis of available studies by increasing the number of studies considered or choosing studies with bigger population.</li><li><b>Ambiguous Claim</b>: The statement that "EDCs influence the expression of genes involved in adipocyte differentiation, such as differentiation inhibitor-3 (ID3)" (Section: Behavioral Patterns and Endocrine Disruptors) is not linked to direct evidence within the manuscript and could benefit from a clearer citation or explanation or reference to the study it was inferred from.</li></ul>	Noted
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.	The references are extensive, relevant, and include recent publications. However, to strengthen the study clinical trials data on gestrinone and drospirenone's use in lipedema or related adipose tissue disorders can be included, if available along with more details and explanation of the hormonal pathways shared between lipedema and gynecological conditions with additional references from recent endocrinological studies.	Ok
Is the language/English quality of the article suitable for scholarly communications?	In general, the quality of language used is spot on and there are no inherent errors. However, there are few words or phrases that are repeated multiple times and the article would benefit from them being altered, either in their wording or their structure.	Ok
<u>Optional/General</u> comments	<p>The manuscript provides valuable insight but could be improved in a few ways. The figures and tables, while helpful, would be more effective with clearer labels, better visual quality, and more detailed descriptions, such as elaborating on the "Common Pathway" in Figure 1. The discussion about gestrinone and drospirenone is interesting but largely theoretical; including clinical trial results or patient data, if available, would make the therapeutic claims more convincing.</p> <p>Adding a "Future Directions" section could highlight specific areas for further research, making the paper more forward-looking.</p> <p>Defining the target audience, such as endocrinologists, gynecologists, or general practitioners, could help make the conclusions more relevant and focused.</p> <p>Additionally, there are a few inconsistencies in formatting, such as citation styles and references, that, if addressed would improve the overall presentation. Finally, while the authors acknowledge the limitations of a narrative review, adding comparisons with systematic reviews or alternative viewpoints could strengthen the manuscript and increase its impact.</p>	Thanks for the valuable comments

PART 2:

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Are there ethical issues in this manuscript?	(If yes, Kindly please write down the ethical issues here in details)	