

## Peer-review Comments and Author Responses

### Reviewer 1

1. *METHODS: When describing the data extraction methodology, consider stating whether blinding was implemented in the different extraction phases. Additionally, elaborate on the nature of discrepancies that require consensus. Were these related to study inclusion, data extraction, or both?*

We thank Reviewer 1 for this comment. We modified the first paragraph of “Data extraction” adding that the reviewers worked blind using Rayyan software. The “Data extraction” paragraph was modified to clarify that this process was done blindly. We included information about the nature of the discrepancies, highlighted in the same paragraph.

2. *RESULTS: It is recommended to review the formatting of Figure 1, “Identification of studies via databases and registers”, as some elements seem to be out of place (arrows and blue boxes overlap).*

We thank Reviewer 1 for this suggestion. Accordingly, we modified the submission of Figure 1 to PNG format to avoid this issue. Figure 1 is sent in PNG format. The references demand minor style revision.

3. *DISCUSSION: It needs minor style revision. It would benefit from a more specific integration of the results, highlighting studies or interventions discussed in the results section and how this review approach is novel, contributing to the existing body of knowledge on the topic. A structured "discussion" model is presented: This mini-review found that ... (add a summary of the important or interesting results). In turn, in agreement with other studies ... Previous evidence has indicated an overall beneficial effect of ... To our knowledge, this is the first mini-review that assessed the ... The present findings are clinically important, notably ... Some controversy exists on ... Further research is thus needed to determine... Limitations must be acknowledged, particularly...*

*Thank you very much for your comment. We agree with your suggestion. We have tried to highlight the most important results in the first paragraph of the discussion. We have also structured the discussion following the model suggested. We have highlighted the strength of our mini-review. The changes are highlighted in yellow. We used the suggested model to improve our discussion. We adjusted the references.*

4. The PCR Journal uses the APA system (see tutorial: <https://www.utoledo.edu/library/help/guides/docs/apastyle.pdf>). For instance, entries in the reference list are arranged in alphabetical order by surname of the first author. Furthermore, place a “.” after the references with a URL. When referencing articles from a journal, include page ranges.

We adjusted the references according to the tutorial.

### Reviewer 2

5. *Mechanism of disease/instrument: I would love to know more about the biological and physiological mechanism by which cellular skin substitutes aid in the healing of diabetic ulcers and could make the introduction more complete since it makes the reader a bit more familiar with the topic.*

Thank you to Reviewer 2 for this suggestion. We agree that adding more information about the mechanisms of how the graft improves the physiology of sick tissue will help to understand how the healing process works. We added two paragraphs in the introduction, the first explaining more about the mechanism of disease and the second one about the mechanism of how skin substitutes work.

### **Reviewer 3**

6. *I wish to draw your attention to a specific area that could benefit from further refinement—the discussion section. I believe there is an opportunity to delve deeper into the implications of your results. The findings, as presented, open the door for exploration and analysis, which, if elaborated upon, could captivate the reader's interest and prompt them to contemplate additional hypotheses. I encourage you to consider expanding upon these intriguing possibilities, offering a more comprehensive discussion that not only elucidates the immediate findings but stimulates intellectual curiosity.*

Thank you, Reviewer 3 for your suggestion. We agree that the discussion section needs improvement. We have made a better discussion structure and added other information that could catch the reader's eye and stimulate curiosity. We used words like: to our knowledge, in this mini-review, controversy, and limitations to make it better structured. We also added data that could help the reader comprehend the discussion easier. The changes are highlighted in yellow.

### **Reviewer 4**

7. *Please consider changing or describing at the beginning of the manuscript (when first used) the term “head-to-head comparison” as I am unsure of its overall meaning. I do not understand if this entails “thorough, complex, in-depth” or what you are referring to.*

We thank the reviewer for this observation and made changes to clarify the meaning. We added an explanation of what we are referring to with this expression highlighted in yellow in the 6th paragraph of the Introduction section.

8. *Grammar and spelling errors are pervasive throughout and need to be addressed. Please consider using Grammarly to review the manuscript. Take an interest in the verb tense used in your entire manuscript.*

We made corrections using Grammarly.

9. *Please review there are no unnecessary blank spaces.*

We have reviewed and removed blank spaces.

10. *Please decide if all paragraphs will have indentation or not. Paragraphs in the introduction, results, discussion & conclusion don't have an indentation, and paragraphs in the methods section do. Change all paragraphs to be the same in format.*

We made changes to address this comment. We standardized the paragraphs by removing the indentations.

*11. Please ensure the images are uploaded using JPEG or supported format, as they are blurry.*  
We will upload it in JPEG format.

*12. Please review your discussion. It should be the most important part of your study. I feel it's a bit "bland". Try to "discuss" more about why these novel treatments that your results have found to be better in outcomes are not widely being used: is it because there is limited awareness by the community, the cost, the regulatory approval by the FDA, the complexity of diabetic foot ulcers themselves, or because many patient-specific factors come into play? Use your opinions as well as the opinion of the expert on the matter. In addition, were there other limitations found in the 22 manuscripts reviewed? Do these skin substitutes present adverse effects, and if so, which ones? It will enrich the discussion and your manuscript overall.*

We agree with the comments. The discussion was enriched with additional information. The added information is highlighted in yellow.