

December 09, 2014



Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 12916-revision.doc).

Title: Smart scaffolds in bone tissue engineering: A systematic review of literature

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Name of Journal: *World Journal of Stem Cells*

ESPS Manuscript NO: 12916

The manuscript has been improved according to the suggestions of reviewers:

1 Manuscript reviewed for grammatical clarity and appropriate vocabulary by a colleague whose native language is English.

2 Format has been updated, "comments" were added.

3 Typesetting were corrected

4 Revision has been made according to the suggestions of the reviewer

(1) Reviewer: 00503904

Comment #1: *The matter of the review is interesting, but in its present form the article is poor. The authors only provide a description of the major finding of several articles, without connecting the results in different studies and without providing their opinion and conclusions from the revised articles.*

Please accept our thanks for your critiques. We have revised the manuscript in accordance with these suggestions and we feel that it is a much better article as the result of these revisions. In addition some grammatical errors were corrected throughout the text. This was the aim of the study to compare and connect the results but the included studies were in vitro studies and their results were not comparable due to variability of methods. Our review could only demonstrate various methods for modification of scaffolds.

Comment #2: *A major effort on editing is also needed to improve grammar and correct many typos.*

Manuscript reviewed for grammatical clarity and appropriate vocabulary by a colleague whose native language is English.

Comment #3: *The results obtained with those materials that have been subsequently tested in animal models need to be commented, to get a view on how fit the results obtained in vitro and in vivo.*

Section "future prospects" was added to discussion to discuss and compare results with in vivo studies.

Comment #4: *Heparin and thrombin are not ECM molecules, please correct this serious error.*

This is very true. These studies were excluded from the ECM table.

Comment #5: Abstract: please clarify which is the meaning of "stabilization of the cells"

The abstract was revised.

(2) Reviewer: 02108906

Comment #1: The authors made the suggestion that *in vivo* and clinical studies need to be performed as a conclusion. However, no further discussion was made on either possible solutions or future direction. Perhaps the authors could discuss a bit more about current animal models for pre-clinical studies, and give some opinions on which modification is most likely to reach clinical translation. For example, both Muschler G.F. et al. and Liu Y. et al. reviewed the animal models for bone tissue engineering and the development of scaffolds for clinical uses in their papers [4,5].

Please accept our thanks for your critiques. We have revised the manuscript in accordance with these suggestions and we feel that it is a much better article as the result of these revisions. In addition some grammatical errors were corrected throughout the text. Section "future prospects" was added to discussion to discuss and compare results with *in vivo* studies. Also, conclusion was revised.

Comment #2: In the tables, it would be more informative if the basic design of the scaffold can be stated, for example, the architecture and fabrication process, which are also critical for cellular responses [6]. In addition, the description for control groups is inconsistent. For some studies, details were given such as "ALP activity: BG+Col-HYA-PS > BG + Col and BG+Col-HYA > BG"; while for other studies, details were omitted and the description were simply given as "control". The detailed description for those control groups are necessary for the context and highly suggested to be added.

Method for preparation of scaffolds varied among included studies. These methods were added to the table. Detailed results and results of control groups added to the tables. However, in some cases no detail was given in the original studies.

Comment #2: Title: The title should use "Bone Tissue Engineering" instead of just "Tissue Engineering" as the review is focused on the former.

The title changed.

Comment #2: Abstract: Besides providing the background information, the introduction could also be presented in a way to provide the motivation of giving this review, followed by the objective. The conclusion should be focused on the findings from reviewed studies, with a minor suggestion on future direction such as animal studies.

Abstract was revised. But journal limited aim section to less than 20 words with no background.

Comment #2: Results: It would be clearer if pie charts can be used to present the number of studies and the distribution of different modification strategies/materials/methods.

This was a great idea. Pie charts were included as figure 2.

Comment #2: Discussion: Using sub headings can make the organization clearer. The tables could be further improved as suggested in Major Points.

Discussion was revised based on major point of the reviewer.

(3) Reviewer: 00545098

In my humble opinion, manuscript might be published as it is.

Thank you again for publishing our manuscript in the *World Journal of Stem Cells*.

Sincerely yours,

A. Khojasteh.

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