Gene, Cell and Tissue
Volume 8 · Issue 4 · e115569

OPEN PEER REVIEW

Fabrication of Poly (Vinyl Alcohol)/Gelatin Biomimetic Electrospun Nanofibrous Composites and Its Bioactivity Assessment for Bone Tissue Engineering

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SUBMITTED	REVISED	ACCEPTED	DOI
8 May 2021	20 Jun 2021	17 Jul 2021	10.5812/gct.115569

About this report

This open peer review (OPR) report shows the public comments made on this article during peer review, by the reviewers, the associate editor and the editor-in-chief, for every revision round, together with the authors' replies. Comments appear only with the consent of the people who wrote them. Reviewers who chose to sign their report are named; the others are shown as "Referee". Comments are edited for language only, and confidential remarks to the editors are not included.

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1 Original submission

3 comments · 18 May 2021 – 26 May 2021

Referee 1 Reviewer

MINOR REVISION 18 May 2021

This article is well explained and documented. I have only a few concerns regarding the paper. Please check for grammatical mistakes, punctuation errors, and incorrectly used verbs or pronouns before submitting the paper. Overall, the paper is well written, and I recommend it for publication after minor revision.
Best wishes,

Associate Editor

MINOR REVISION 23 May 2021

Dear editor
The manuscript is suitable for publication after minor revision according to the reviewers' comments.
Best regards

Editor-in-Chief

MINOR REVISION 26 May 2021

Based on the reviewer's comments and my reading of the manuscript, this manuscript needs minor revision. Please revise it carefully and reply to the comment.

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Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Dear editor we do all comment exactly and highlighted them in the text.

Reviewer 1: green font
1- There are some grammatical errors in the manuscript.

All three respected reviewers requested grammatical corrections; the editorial corrections are marked in the text in red font.

2- The discussion section is poor and there is no comparison between other studies.

Hence, in some previous studies, the preparation and utilization of PVA/GE scaffolds have been reported. Ceylan and coworkers (25) prepared the PVA/GE cryogels by chemically and physically crosslinking of PVA and gelatin mixture. They demonstrated the physically crosslinked cryogels degraded faster than the chemically crosslinked ones. While, the scaffolds crosslinked physically showed better biocompatibility.

3- there are no references in some sections especially in the discussion.

References added to the text of the article:

24. Hanna H, Mir LM, Andre FM. In vitro osteoblastic differentiation of mesenchymal stem cells generates cell layers with distinct properties. *Stem Cell Research & Therapy*. 2018; 9: 203. Doi:10.1186/s13287-018-0942-x

- Ceylan S, Göktürk D, Bölgen N. Effect of crosslinking methods on the structure and biocompatibility of polyvinyl alcohol/gelatin cryogels. *Bio-Medical Materials and Engineering*. 2016; 27 (4): 327–340. Doi: 10.3233/BME-161589

26. Linh NTB, Min YK, Song H-Y, Lee B-T. Fabrication of polyvinyl alcohol/gelatin nanofiber composites and evaluation of their material properties. *Journal of Biomedical Materials Research Part B: Applied Biomaterials*. 2010; 95 (1): 184-191. Doi: 10.1002/JBM.b.31701

27. Linh NTB, Lee B-T. Electrospinning of PVA/gelatin nanofiber composites and crosslinking for bone tissue engineering application. *Journal of biomaterials applications*. 2012; 27 (3): 255-266. Doi: 10.1177/0885328211401932

References added to the supporting information:

6. Van de Loosdrecht AA, Beelen RHJ, Ossenkoppele GJ, Broekhoven MG, Langenhuijsen MMAC. A tetrazolium-based colorimetric MTT assay to quantitate human monocyte mediated cytotoxicity against leukemic cells from cell lines and patients with acute myeloid leukemia. *Journal of Immunological Methods*. 1994; 174: 311-320. Doi: 10.1016/0022-1759(94)90034-5

4- This manuscript is very similar to the article doi.org/10.1177/0885328211401932. The author should discuss it and only glutaraldehyde treatment is different.

Also, Linh and Lee (27) produced the electrospun nanofibrous PVA/GE that was physically crosslinked by methanol treatment. They seeded MG-63 cells on the manufactured scaffold and showed that osteoblasts could attach and proliferate on the nanofibrous PVA/GE. The aim of this study was to fabricate the biocompatible PVA/GE nanofibrous scaffold for osteogenic differentiation of MSCs.

5- In the figure of the MTT test, it's better the curve presented by percentage.

Figure 5a

Reviewer 2: blue font
1- prepare the MTT curve based on the cell viability.

Figure 5a

2- The writing quality must be improved.

All three respected reviewers requested grammatical corrections; the editorial corrections are marked in the text in red font.

3- please mention the corresponded concentration of the MTT solution.

The optical density (OD) corresponds to the viable cell numbers that were cultured on the crosslinked scaffolds and control samples (The control group was cell seeded over the cell culture plate). After being sterile, crosslinked PVA/GE scaffolds were placed in a 24-well culture plate and seeded with a cell density of 2×10^4 cells/well and maintained at 37 °C, 5% CO2 under 200µl DMEM with 20% FBS. During the test, the culture medium was replaced every 2 days. After 3, 5, and 8 days of cell seeding respectively, the medium culture was replaced with PBS solution (0.01 M, pH 7.4) for washing the dead cells on the scaffold, and DMEM containing 10% MTT solution (with concentration level 5 mg/ml) was freshly added to each culture well and the cultures were incubated at 37 °C and 5% CO2 for 4h.

4- please explain how the crosslinked scaffold can improve cell viability?

Due to presence of the numerous polar groups in the PVA and gelatin structures, they are known as hydrophilic polymers. Therefore, scaffolds containing PVA/GE can be destroyed and dissolved easily in aqueous solutions (such as PBS). However, crosslinking lead to the formation of a 3-D network of polymers, that can provide a stable environment for adhesion and proliferation of seeded cells.

5- please explain your study differences or probably similarity with this study: "Fabrication of polyvinyl alcohol/gelatin nanofiber composites and evaluation of their material properties, https://doi.org/10.1002/jbm.b.31701".

Besides, Linh et al. (26) fabricated PVA, GE, and PVA/GE nanofibers by electrospinning. They investigated the effect of process parameters (including the concentration of GE in PVA/GE blends, electrical field, and tip-to-collector distance) on the chemical, morphological, and mechanical properties of the prepared scaffolds.

The aim of this study was to fabricate the biocompatible PVA/GE nanofibrous scaffold for osteogenic differentiation of MSCs.

Reviewer 3:
This article is well explained and documented. I have only a few concerns regarding the paper, please do check the grammatical mistakes, punctuation error and verb or pronouns if they add incorrectly before the submission of the paper. Overall the paper is well written and I recommend it for publication after minor revision.

Best wishes,

All three respected reviewers requested grammatical corrections; the editorial corrections are marked in the text in red font.

[Translated from Persian by the Brieflands editorial office.]

2 Revision 1

4 comments · 27 Jun 2021 – 17 Jul 2021

Referee 1 Reviewer

ACCEPT 27 Jun 2021

The revised manuscript has been improved, and I wish the authors all the best.

Referee 2 Reviewer

ACCEPT 29 Jun 2021

In this format, this article could be accepted. But there is no MTT curve based on cell viability in Fig5a.

Associate Editor

ACCEPT 17 Jul 2021

Dear Dr. Asadollah Asadi,

It is our pleasure to inform you that the mentioned article has been accepted for publication in the journal.
Below you can find final comments by our peer reviewers.
Final Reviewers' Comments:
Reviewer 1:
The revised manuscript has been improved, and I wish the authors the best.
Decision: Accept
Reviewer 2:
In this format, this article could be accepted. But there is no MTT curve based on cell viability in Fig5a.
Decision: Accept
Reviewer 3:
All comments were properly addressed in the revisions.
Decision: Accept

Yours sincerely

Bita Moudi, PhD
Associate Editor
Gene, Cell and Tissue

Editor-in-Chief

ACCEPT 17 Jul 2021

Based on the reviewer's and AE's comments, the revisions were carried out well. Thus, this manuscript can be accepted for publication in GCT.