

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67042

Title: Effect of glycyrrhizic acid and 18 β -glycyrrhetinic acid on the differentiation of human umbilical cord-mesenchymal stem cells into hepatocytes

Reviewer's code: 05935626

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: Indonesia

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-18 16:22

Reviewer performed review: 2021-04-19 17:17

Review time: 1 Day

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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SPECIFIC COMMENTS TO AUTHORS

I would like to congratulate the authors for this manuscript. This study is interesting, current and brings new perspective. I have some comments about the manuscript:

Material and methods: Ethics committee approval and human umbilical cord collection: Please check your uploaded ethics review board approval certificate because the name of the chairperson who signed the certificate is missing. Please refer related previous study on the methods that you use. Please meet the requirement of using SI units.

Processing and culturing of human umbilical cord tissue using explant culture: Fig. 1A is missing. Please explain how did you distribute P1 to P4 cells into the treatment groups. Please clarify if there is any special appointment of certain P1 to P4 cells into certain treatment group.

Statistical analysis: Please provide the biostatistics review certificate signed by a biostatistician.

Discussion: Regarding the use of P1 to P4 MSCs as stated in the methods on page 6, please explain your reasons of using multiple passage cells. Please point out the limitations of your study within the methodology.

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67042

Title: Effect of glycyrrhizic acid and 18 β -glycyrrhetic acid on the differentiation of human umbilical cord-mesenchymal stem cells into hepatocytes

Reviewer's code: 05817430

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Research, Research Scientist

Reviewer's Country/Territory: Iran

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-13 11:27

Reviewer performed review: 2021-04-25 05:39

Review time: 11 Days and 18 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In the present research paper, the authors present the “Effect of Glycyrrhizic Acid and 18 β -Glycyrrhetic Acid on the Differentiation of Human Umbilical Cord Mesenchymal Stem Cells into Hepatocytes”. In detail, the work is well done, but I have some major concerns about the paper which are listed as follows: • There are some grammatical errors in the text. Please control the text in that manner. For example: “Considering the characteristics of these compounds in hepatic anomalies, in this study, we hypothesized that these triterpenes may have the ability to differentiate hUC-MSCs into hepatocytes directly or aid in the process of differentiation.” • Also please modify the text as follows: “human umbilical cord derived MSCs (hUC-MSCs)” should be “human umbilical cord-MSCs (hUC-MSCs)”. • Please modify the title as follows: Effect of glycyrrhizic acid and 18 β -Glycyrrhetic acid on the differentiation of human umbilical cord-mesenchymal stem cells into hepatocytes • Also you can modify the running title as follows: Differentiation of MSCs in to the hepatocytes • Please modify the keywords as follows: glycyrrhizic acid; 18 β -glycyrrhetic acid; hepatocyte differentiation; human umbilical cord-MSCs • The abbreviations must be clarified and mentioned in the same format in the text. For example: - glycyrrhizic acid and 18 β -glycyrrhetic acid (abstract). - MTT (Method). • In addition, the figures and error bars shown are not at high resolution and not correctly focused to enable detailed scrutiny.

PEER-REVIEW REPORT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67042

Title: Effect of glycyrrhizic acid and 18 β -glycyrrhetinic acid on the differentiation of human umbilical cord-mesenchymal stem cells into hepatocytes

Reviewer's code: 04609834

Position: Editorial Board

Academic degree: DDS, PhD

Professional title: Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-13

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-04-17 16:16

Reviewer performed review: 2021-04-25 15:03

Review time: 7 Days and 22 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

In this manuscript, the authors first proposed the hypothesis that glycyrrhizic acid (GA) and 18 β -glycyrrhetic acid (GT) may have the ability to differentiate human umbilical cord derived mesenchymal stem cells (hUC-MSCs) into hepatocytes directly or aid in the process of differentiation. On this basis, a series of experiments were designed. Firstly, hUC-MSCs were extracted and cultured. Then, MTT was used to determine the appropriate acid concentration to induce cell differentiation. Finally, gene expression, protein expression and periodic acid Schiff staining were used to evaluate the differentiation results. Overall, the research design was clear, and the experiment was complete. There are some small problems that need to be improved. 1. The paragraph 2 of the “material and methods” mentioned “Fig 1A”, but this figure did not shown in the paper. Please revise this section. 2. Some raw data are not present such as the stained orifice diagram. 3. There is room for improvement in English. Some descriptions in the manuscript are vague and potentially misleading.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Stem Cells*

Manuscript NO: 67042

Title: Effect of glycyrrhizic acid and 18 β -glycyrrhetinic acid on the differentiation of human umbilical cord-mesenchymal stem cells into hepatocytes

Reviewer's code: 05817430

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Research, Research Scientist

Reviewer's Country/Territory: Iran

Author's Country/Territory: Pakistan

Manuscript submission date: 2021-04-13

Reviewer chosen by: Li-Li Wang

Reviewer accepted review: 2021-07-29 18:26

Reviewer performed review: 2021-08-02 04:42

Review time: 3 Days and 10 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS



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In the present study, the authors represent the revision for "Effect of Glycyrrhizic Acid and 18 β -Glycyrrhetic Acid on the Differentiation of Human Umbilical Cord-Mesenchymal Stem Cells into Hepatocytes". There is no problem, but the paper can be accepted after the important revision as follows: Figures: The error bars and the text on the (Figures) shown are not at high resolution. Please modify the figures. Finally, after the modification of figures, the paper can be accepted.