



## PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 58626

**Title:** Umbilical Cord Derived Mesenchymal Stem Cells Preconditioned with Isorhamnetin: Potential Therapy for Burn Wounds

**Reviewer's code:** 02629733

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Professor

**Reviewer's Country/Territory:** Lebanon

**Author's Country/Territory:** Pakistan

**Manuscript submission date:** 2020-07-30

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2020-08-04 09:24

**Reviewer performed review:** 2020-08-17 10:33

**Review time:** 13 Days and 1 Hour

<b>Scientific quality</b>	<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 Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

Results carried to Discussion. Define terms (like complete remodeling) Needs some English editing



### PEER-REVIEW REPORT

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 58626

**Title:** Umbilical Cord Derived Mesenchymal Stem Cells Preconditioned with Isorhamnetin: Potential Therapy for Burn Wounds

**Reviewer's code:** 02567167

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** Spain

**Author's Country/Territory:** Pakistan

**Manuscript submission date:** 2020-07-30

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**Review time:** 31 Days and 19 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	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**

The paper by Aslam et al. entitled "Umbilical Cord Derived Mesenchymal Stem Cells Preconditioned with Isorhamnetin: Potential Therapy for Burn Wounds" shows how preconditioning hU-MSCs with the flavonoid isorhamnetin improves their ability to promote burn healing in an animal model. Based on histological and gene expression studies, the authors conclude that the treatment improves healing due to the anti-inflammatory and tissue remodelling inducing effect of preconditioned hU-MSCs. The study is interesting and supports the application of MSCs in cell therapy for the treatment of skin wounds. Remarks: 1- The authors should explain in the introduction why they selected isorhamnetin for study. Furthermore, in the discussion they should attempt to associate the observed effects of MSC preconditioning with this flavonoid. 2- Materials and methods. The details of isolation of hU-MSCs from human umbilical cord explants should be explained in more detail: size of the explant, incubation time, etc. 3- Materials and methods. hU-MSCs have been characterized by surface markers, but in addition their ability to differentiate into osteoblasts, adipocytes and/or chondrocytes should have been demonstrated. 4- Materials and methods. The number of animals used in each treatment group should be included. 5- Results. 5  $\mu$ M isorhamnetin concentration did not affect MSC viability, but 10  $\mu$ M reduced it by approximately 50%. Have the authors tested concentrations lower than 5  $\mu$ M? 6- Results. Figure 3, scratch images are difficult to interpret. The authors should show images of the cultures at lower magnifications. 7- Results. Figure 4. Why does the wound of the IH+MSCs group appear from day 1 surrounded by hair and the other two groups appear shaved?. Has the same methodology been used for all groups? 8- Results. The indication of the statistical significance in figure 3H and especially in figure 6 is very confusing. The text in the figures does not indicate with respect to which treatment the differences are



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significant. For example, in figure 6F, all the columns are marked with \*\*\*. 9- Discussion. The histological analysis part is more a repetition of results than a discussion. The authors should correct this. 10- Discussion. Authors should clarify sentences that create confusion: - They claim that IL-1 $\beta$  and IL-6 were upregulated at day 7 and 14, but then they write: "Their expression levels were decreased as the wound healing progresses." - In page 23, the authors write: "In contrast, the expression level of Bcl-2 was reduced after 7 days of burn infliction and significantly lower expression was observed as the wound progresses". However, after 14 days, it can be seen in Figure 6 that it only decreases with IH-MSc treatment. The authors should explain what they mean. - In page 23, the authors write: "the expression of Bax was extensively reduced at day 7 and day 14 post burn injury, and Bcl-2 level was elevated as compared to the burn wound control". As shown in figure 6, the expression of Bcl-2 at day 14 in IH+MSCs is lower than in the control. Therefore, the authors should correct the commentary. 11- It would be interesting that the authors had studied, in addition to gene expression, the protein expression of inflammatory and remodeling cytokines in wound samples, in order to obtain more robust conclusions.