

Letter to the editor

A response to article “Java sea *Spirulina platensis* chemical analysis and its protective ability against H₂O₂-exposed umbilical cord mesenchymal stem cells according to CD73, CD90, and CD105, viability, and HIF-1 alpha docking”

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DEAR EDITOR

We are grateful to the authors whose work was reported in the Journal of Applied Pharmaceutical Science Vol. 12(09), pp 067–075, September 2022 with the title “Java Sea *Spirulina platensis* chemical analysis and its protective ability against H₂O₂-exposed umbilical cord mesenchymal stem cells (MSCs) according to CD73, CD90, and CD105, viability, and HIF-1 alpha docking” (Priyanti *et al.*, 2022). This is very important information about the effect of *Spirulina platensis* on H₂O₂ exposure which tends to increase MSC viability.

We would like to give our thoughts, particularly on the characterization method of MSCs in this study. We highly regarded the author’s use of stemness markers of MSCs like CD73, CD90, and CD105, and hematopoietic markers (CD45, CD34, CD11b, CD19, and HLA-DR) to characterize MSCs culture. Unfortunately, this study did not report on the differentiation ability of MSCs.

Based on The International Society for Cellular Therapy, there are three criteria to define MSCs. First, MSCs must be adherence to tissue culture flasks. Second, MSCs must express CD105, CD73, and CD90 and must lack expression of CD45, CD34, CD14 or CD11b, CD79a or CD19, and HLA class II as measured by flow cytometry. Third, the cells must be able to differentiate into osteoblasts, adipocytes, and chondrocytes

(Dominici *et al.*, 2006). So, it is important to check the potential differentiation ability of MSCs.

In the Discussion, the authors said that “Some studies gave positive results in overcoming oxidative stress using the 125 ng/ml *Spirulina* (SP) extract.” But there are no references included. Tajvidi *et al.* (2021) reported that prior to obtaining the final extract concentration, it is preferable to perform an MTT cytotoxicity assay using SP or *Arthrospira platensis* aqueous extract concentration that was toxic to 50% of the cells to get IC₅₀. Then the extract was used at concentrations of 129.5 µg/ml and 366.4 µg/ml to treat the human Caucasian non-small-cell lung adenocarcinoma A549 cell line and human foreskin fibroblast (HFF) cell lines respectively for 24 hours (Tajvidi *et al.*, 2021).

Furthermore, the justification for using final H₂O₂ concentrations of 100 and 300 µM should be explained. Facchin *et al.* (2018) reported that H₂O₂ was used to compare the behavior of human Wharton’s jelly-derived MSCs and human adipose tissue-derived stem cells in response to oxidative stress at various concentrations (ranging from 50 to 400 µM) and time exposures (1 or 2 hours) (Facchin *et al.*, 2018). Saleem *et al.* (2021) also reported that human bone marrow stem cells were exposed to progressively higher concentrations of H₂O₂ 125, 250, 500, 750, and 1000 µM in DMEM with 1% FBS at 37°C with 5% CO₂ for 2 hours in order to establish the oxidative stress model (Saleem *et al.*, 2021).

As for the molecular docking results, we checked the PDB ID for HIF protein (5LAS) on the PDB database and found that this protein has two unique ligands, N-Oxalylglycine (ID OGA) and manganese ion (ID MN). However, the authors did not explain why N-Oxalylglycine was not used in the docking step as a control despite the presence of 3,4-OH-benzoic acid in the SP extract. Since there are two binding areas proposed for HIF-1,

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the authors should also clearly state the native ligands used as a control for the active binding site and the DNA binding domain respectively along with their key amino acid residues implicated in the interaction and whether these residues match those in their corresponding native ligand. The information on which compounds interact in the binding site and which one in the DNA binding domain should be provided because the paper only mentioned phycocyanobilin in the DNA binding and canthaxanthin in the active binding sites. The interaction for other compounds in the SP extract should also be described.

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AUTHOR CONTRIBUTIONS

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agreed to be accountable for all aspects of the work.

ETHICAL APPROVALS

Not applicable.

DATA AVAILABILITY

All data generated and analyzed are included in this research article.

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DISCLOSURE

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