Reviewer’s report

Title: Astaxanthin mitigates cobalt cytotoxicity in the MG-63 cells by modulating the oxidative stress

Version: 0 Date: 18 Jan 2017

Reviewer: Balmiki Ray

Reviewer’s report:

The authors have used cell culture model to demonstrate the beneficial effects of ASX in cell culture model. The findings may be too preliminary to be convinced about any beneficial effects of ASX in the treatment of metal-on-metal bearing toxicity as seen after major joint replacement surgery

Abstract: Concise and to-the-point

Introduction: 1) There are grammatical errors that can be fixed. For example: "caused the generation metal particles and ions"- may be replaced by "caused the generation of metal particles and ions"; Another one:- "small amount of cobalt ion in the human body is essential to good health"; 'to' may be changed by 'for'. "Cobalt ion was found at MoM patients` whole blood or serum": "at" may be changed by "in"

2) Have Cr and Co in parenthesis when cobalt and chromium terms are first introduced.

3) Line 40: Mention briefly the full form of CSF and RANKL

4) The authors have treated MG-63 cell line with ASX. As a rationale, the authors just mentioned about the anti-inflammatory, antioxidant property observed in one study [24]. This is not sufficient to justify the rationale for using ASX in the study. The authors need to add more research evidence of the utility of ASX as anti-inflammatory, antioxidant and immune-modulant.

Methods: 1) Give the full form of ATCC

2) Add another paragraph describing MG-63 treatment conditions. What are the doses of Co and ASX? How long was the treatment etc.

Results: 1) Co-induced significant (50%) cytotoxicity was observed with a Co conc. of 200μM. Is that conc. physiological?

2) Fig. 1B: Indicate the conc. unit of ASX in the figure.
3) Fig. 1D: Western blots figures are not very convincing. The bands for cas-3 don't show too much of a difference between 1, 5 and nm of ASX. Similar comment for fig. 2A. Also please indicate how many times the experiments were repeated.

4) Did the authors use any known antioxidant or a chelating agent to compare the results vs. ASX?

Discussion: Too concise. The authors need to discuss about the molecular pathways related to metal toxicity with a focus on JNK, Bcl, NGkB etc.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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