Author's response to reviews

Title: Evaluation of Wound Healing and Invivo anti-inflammatory Activity of Rhizomes of Rumex abyssinicus J. in Mice

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Dear reviewers, first of all we would like to acknowledge you for your time and dedication to revise our manuscript entitled “Evaluation of Wound Healing and Invivo anti-inflammatory Activity of Rhizomes of Rumex abyssinicus J. in Mice”. We made correction based on your comments and the responses are as follows.

RESPONSE TO REVIEWERS
1. REVIEWER ONE
Reviewer's report
Title: Evaluation of Wound Healing and Invivo anti-inflammatory Activity of Rhizomes of Rumex abyssinicus J. in Mice
Version: 4 Date: 27 February 2015
Reviewer: Andrea Aro
Reviewer's report:
Major Compulsory Revisions:
The purpose of the study was to evaluate the potential activity of the Rhizomes of Rumex abyssinicus J. in wound healing and inflammation. Considering that the subject of the manuscript is very interesting, I believe that additional analyses should be included to become the manuscript more consistent and appropriate for publication.
• The aim of the study was to prove the traditional claim of the plant for wound healing and inflammation. Many literatures correlate efficacy of traditional plant for wound with wound contraction, epithelization, tensile strength and hydroxyproline measurement. And also we have done anti-inflammatory activity of the plant as support for wound healing activity. Thus, we use the two models (excision and incision) as baseline for testing of wound healing.
• Explained in discussion…line 333 to 338
Abstract section:
1) The tissue that was analyzed was not cited in the abstract. Please, include this information in this section and in the title of the manuscript.
   • Described …line 49
2) The analyses that were used for the characterization of the healing activity of the plant in vivo were not described in this section. This information with the respective result could become the data more interesting if it was included.
   • Described…line 54 to 57
   • Since there is p-value we don’t think it is necessary to include other numbers
Introduction section:
1) Line 61: correct the word “coomon” for “common”
   • Corrected…line 64
2) Line 67: the correct form is “at least”
   • Corrected…line 81
3) A description of the main molecular events of the wound healing in skin should be included, such as the collagen synthesis, pro-inflammatory cytokines participation and biomechanical aspects of the tissue during this process. These informations could clarify the choice of the techniques used for the evaluation of the healing potential of the plant and facilitating the data discussion.
   • Added …line 67 to 76
Result section:
1) Please, include the time of wound healing process that was analyzed in each table.
   • Just when we analyze the time of healing within a group we didn’t get significant difference, it is closer to one another. Therefore, we prefer not to include it.
M & M section:
1) Why animals of either sex were used? I believe that the hormonal variation of the female can interfere in the result, especially when it is compared with the result from male animals.
   • Of course there may be influence of hormones but the animals were first wounded and randomly assigned to different groups to avoid such influence
2) Please, describe the composition of the base of the ointment.
   • Described…line 165-155
Discussion section:
1) (Line 324): It is very speculative to attribute the role of R. abyssinicus in the increasing in percentage closure of excision wounds as a result of the induction
of macrophage cell proliferation, since no test was done for this. Various other components of the extracellular matrix have to be produced to close the excision wounds that should be considered in the discussion of this result.

- macrophage cell proliferation effect of the plant was done by Getie et al on the plant...reference 21

2) (Line 304): Likewise, it is not possible to suggest that the plant has the ability to facilitate the proliferation of epithelial cells, enhancing wound contraction by enhanced epithelial migration. Histological analysis should be done for evaluate this result.

- Deleted ....line 332

3) (Line 314) “by removing unwanted things”...what does it mean?

- Deleted and modified...line 340

4) (Line 359) “the extract could be the result of its ability to inhibit the action of bradykinin and/or prostaglandins” ...again is very speculative.

- It is not speculative

- we searched a literature and explained the phases of inflammation in paragraph from line 348-356 and our extract was found to have an effect almost similar with standard drug indomethacine. Thus, we try to correlate the finding based on evidences.

5) (Line 366) “The probable explanation for increased tensile strength could be due to the increase in both remodeling of collagen, and the formation of stable intra- and intermolecular crosslink”...why a simple staining with HE or some more appropriate dye for the observation of collagen organization (Ponceau S, ponceau SS, xylidine ponceau) was not done? A simple analysis under light microscopy could be done to prove the result, improving largely the data discussion.

- Thank you. we prefer to delete this justification since we didn’t do collagen organization or there was no report on effect of the plant on collagen....line 366

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests.

2. REVIEWER TWO

Reviewer's report

Title: Evaluation of Wound Healing and Invivo anti-inflammatory Activity of
Rhizomes of Rumex abyssinicus J. in Mice
Version:4 Date:20 March 2015
Reviewer: Priyanga Ranasinghe
Reviewer's report:
Minor Revisions - The language in the manuscript requires significant improvement. Numerous typographical and grammatical errors are present throughout the manuscript. Suggest to get the manuscript corrected by an English speaking person/expert if possible
• Edited
Level of interest: An article of importance in its field
Quality of written English: Needs some language corrections before being Published
• Corrected
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:
I declare that I have no competing interests
3. REVIEWER Three
Reviewer's report
Title: Evaluation of Wound Healing and Invivo anti-inflammatory Activity of Rhizomes of Rumex abyssinicus J. in Mice
Version:4 Date: 22 March 2015
Reviewer: Mary T. “Terry” Loghmani
Reviewer's report:
Thank you for the opportunity to review this manuscript submission. The topic is interesting and potentially of scientific merit and importance; however, as it is written I am unable to make a recommendation for publication. I have attached the document with some of my edits and comments. This is not an exhaustive edit, nor is it meant for public access; however, it is more thorough and specific than what is listed below, and it may prove of some benefit to the authors.
Major Compulsory Revisions
Some major compulsory revisions will need to be made to determine the appropriateness of this manuscript for publication.
It needs to be re-written with grammar and spelling errors corrected to make it easier/possible for the reader to follow.
• Corrected
• Your corrections were incorporated and highlighted
The title needs to more directly reflect what has been found by this research
• The research found wound healing of the plant and confirmed in vivo anti-inflammatory activities. Thus, these suggestion is not clear for us

The purpose and design needs to be more clearly described to make the research procedures and related findings more decipherable.
• Rephrased and corrected

The type of wound(s) under consideration needs to be specified clearly. The types of treatments and their rationale for selection were not clearly described. Of significant concern, is that the research groups need to be clearly defined, and better rationales provided for the difference in the types of animals for the different experiments and the methods/rationale for the outcomes selected. A chart listing the groups may help with this. Presenting the data as graphs with significance differences between groups would be helpful to more quickly interpret the findings. This needs to be tied to the discussion. Limitations need to be listed.
• The groups were clearly defined …line 184 to 185 (table added)
• We use rats for skin irritation study because we can easily observe the effect on rats than mice
• Reason for selection of the two methods was described in the discussion…line 33-338

Overall, there needs to be greater clarity, consistency and coherence between all elements of the manuscript in order for its scientific merit to be better communicated and evaluated.

I could not find several of the references, either because my library does not have access to some/many of the journals or the references were from a book, or of significant concern, is that some of the articles simply could not be found on PubMed as cited.
• MOST OF THE REFERENCES’ JOURNAL WERE NOT INDEXED IN PUBMED

Minor Essential Revisions

Figures of the wound healing between groups would be very helpful and interesting. I could not fully discern if the authors were building on some of their own, previous work. In conclusion, since traditional plant-based medicine could have significant global health implications, and their efforts/interest in this area are commendable, I would encourage the authors to revise and re-submit.

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Not suitable for publication unless extensively edited
Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.
Declaration of competing interests:
'I declare that I have no competing interests'