Author’s response to reviews

Title: Crude extract from Libidibia ferrea Linn leaves decreased intra articular inflammation induced by zymosan in rats

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Dear Editor,

We are submitting a revised version of our manuscript entitled “Crude extract from Libidibia ferrea Linn leaves decreased intra articular inflammation induced by zymosan in rats”, according to your and the reviewers’ comments and suggestions.
We provided point-by-point responses to the Editor and reviewers’ comments below. We would like to thank you and the reviewers for taking the time to read and suggest modifications to our manuscript. The suggestions and feedback have been very useful to improve the quality of our article.

With best regards,

Aurigena Antunes de Araújo

Corresponding author (On behalf of the authors of the manuscript)

Editor Comments:

1. The reason for choosing the dosages of the experimental drugs (Zymosan, diclofenac, LfAE).

Response: The dosages of the experimental drugs (Zymosan, diclofenac, LfAE) were based on previous studies reported in the literature (Ferreira et al., 2014; Guerra et al., 2016). This information is now in the manuscript (materials and methods section) and the references were added to the reference list.


2. The number of rats for each group?

Response: Five (n=5) rats were used per experimental group, according to a description of previous studies (Guerra et al., 2016).

3. When the synovial fluid and tissue were collected?
Response: The synovial fluid and tissue were collected 24 hours after the induction of arthritis. This information has been added to the manuscript.

4. I recommend that the name of positive control should be changed
Response: The name of positive control was changed, according to your comment: positive control= zymosan control.

5. The IL-1Beta and TNF-alpha: Make sure the sensibility or lower limit of detection.
Response: We confirmed the values of sensibility or lower limit of detection through the manufacturer.

“Levels of IL-1β (detection in the range: 62.5–4000 pg/mL; sensibility or lower limit of detection: 12.5 ng/mL of recombinant mouse IL-1β), and TNF-α (detection range: 62.5–4000 pg/mL; sensibility or lower limit of detection: 50 ng/mL of recombinant mouse TNF-α) in the synovium samples were determined with a commercial ELISA kit (R&D Systems, Minneapolis, MN, USA).”

6. Histopathological analysis: One figure for control and vehicle is enough.
Response: As suggested, the figure of the histopathological analysis was modified.

Reviewer 2:
1. Abstract needs to be re-written as some of the information is not clear. For e.g. authors mentioned "Cell counts, histopathological analysis, and inflammatory cytokines (IL1-beta and TNF-alpha) were performed". How they measured IL-1b and TNF-a are not clear.
Response: The abstract was rewritten. The inflammatory cytokines were performed by Enzyme-Linked Immunosorbent Assay
2. Language needs to be improved with a special focus on grammar and flow of sentences. The complex sentences in the results in abstract, introduction and discussion must be re-written in simple to track the information. This will also help in delivering clear information as well.

Response: We have carefully revised the entire manuscript, according to your comment.

3. The traditional uses of L. ferrea focusing on rheumatoid arthritis needs to be expanded.

4. In the figure legends, authors need to confirm whether they performed One or Two-way ANOVA

Response: Two-way ANOVA was performed.

5. Overall it seems that the extract doesn't have any dose-dependent effects. Authors need to explain.

Response: The manuscript demonstrates that the extract does not have any dose-dependent effects. We have carefully revised the entire manuscript according to your comment to make this clear.

6. Several incomplete sentences are in the discussion section. Authors need to pay attention to it and simplify the sentences.

Response: We have carefully revised the discussion section according to your comment.

7. Author should write a concise, focused and clear discussion rather than repeating the results

Response: We have carefully revised the discussion section according to your comment.