Author’s response to reviews

Title: Inhibition of biofilm formation in Mycobacterium smegmatis by Parinari curatellifolia leaf extracts

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Author’s response to reviews:

a) My main concern is the choice of test organism for this study. The authors need to extensively justify their choice in order to substantiate the data generated in this study. The following highlighted are obtained from publish literature. M. smegmatis is generally considered a non-pathogenic microorganism; however, in some very rare cases, it may cause disease. Even though M. smegmatis offers some technical benefits such as a shorter generation time and negligible risk to laboratory workers, it is significantly less effective in the detection of anti-M. tuberculosis compounds relative to M. bovis BCG. This limitation needs to be taken into consideration when selecting an in vitro screening model for tuberculosis drug discovery.


Response: Mycobacterium smegmatis has been said not to be a suitable surrogate model for M. tuberculosis by the above papers. However, many other papers also support the use of M. smegmatis as a model for M. tuberculosis. A paper by Thi et al., 2010 supports the idea of the potential use of M. smegmatis for the development of TB vaccine candidates. Another paper by He and De Buck (2010) also states M. smegmatis as a model to investigate mycobacterial physiology. Mycobacterium tuberculosis is a slow growing and pathogenic organism, therefore other model mycobacterial species that are rapidly growing and non-pathogenic are usually used in its place when screening for antimycobacterial activity of plant extracts. Mycobacterium
smegmatis is an example of a model mycobacteria and is used as a test organism in the initial primary screening process while Mycobacterium tuberculosis is usually used at a later stage for further studies. M. smegmatis has been shown to have a similar drug sensitivity profile to that of Mycobacterium tuberculosis. This was why we chose the species for use in our study for in vitro screening model for tuberculosis drug discovery.


He and De Buck Cell wall proteome analysis of Mycobacteriumsmegmatis strain mc2 155 BMC Microbiology 2010, 10:121

b) M. smegmatis is significantly less effective in the detection of anti-M. tuberculosis compounds relative to M. bovis BCG. This limitation needs to be taken into consideration when selecting an in vitro screening model for tuberculosis drug discovery.

Response: M. smegmatis can induce cytokine production by macrophages better than pathogenic mycobacterial species (1) and can activate and induce the maturation of dendritic cells better than BCG by upregulation of major histocompatibility complex (MHC) class I and costimulatory molecules (2). M. smegmatis can also access the MHC class I pathway for presentation of mycobacterial antigens more efficiently than BCG (3).


c) The presentation of the data are redundant in many cases. For instance, Table 1 has the same data/information as Fig. 1, 2, 3 and 4. In my own opinion, the presented microplate image is not relevant.

Response: Table 1 has been removed as it was duplicating information given by Fig 1, 2, 3 and 4. The microplates have been removed.
d) Figs. 5-8: appears too busy, please clearly amend and correct as necessary. Remove redundant images.

Response: The crystal violet stained microplate was added to show readers a pictorial image of the results but they have been removed in Figures 5 and 6. We have deleted Figure 7.

e) In the discussion, there are too much sweeping statements. There are also a number of speculation which has no references to substantiate it. I have highlighted a few of such concerns in the attached PDF. However, the authors need to critically go through the whole content and amend accordingly. I will also implore the authors not to directly translate 'antimycobacterial' activity = anti-tuberculosis based on the fact that the strain used in this study is not pathogenic (see my earlier comments). This use of statement was made in the results and discussion sections.

Response: We have corrected the manuscript as per the recommendations.

Reviewer 3: Reviewer comments

Abstract:

1. The abstract is rather too long. Please read the instruction to authors regarding writing an abstract and do the necessary changes.

Response: We have reduced the abstract from 382 words to 310 words.

2. Scientific names should be abbreviated at their first mention along with their full names. Eg; Mycobacterium smegmatis (M. smegmatis)... Parinari curatellifolia (P. curatellifolia)... Mycobacterium tuberculosis (M. tuberculosis). Further mentions can be written in abbreviated forms.

Response: We have corrected this in the text.

3. Grammatical and typographical errors need to be rectified.

Response: We have corrected the errors.

Background:

4. Technical names should be abbreviated at their first mention along with their full names. Eg; Tuberculosis (TB)... Multi-resistant Tuberculosis (MTB) etc. Further mentions can be written in abbreviated forms.

Response: We have corrected this in the text.
5. The background section too seems to be lengthy. There is so much mention on the theory of tuberculosis infection, which could be cut down.

Response: We have cut down the background from 1326 to 905 words and reduced the content of the theory of tuberculosis.

6. The language needs to be corrected with the help of a native English speaker. Response: We have corrected the language.

7. The authors fail to introduce the significance of using M. smegmatis in the study. This should be rectified.

Response: We have corrected this in the text.

8. The background should mention the important phytochemicals reported from the plant previously.

Response: We have corrected this and highlighted the corrected text in red.

Methods, Results and Conclusion:

9. Plenty of grammatical errors and spelling errors are found throughout the section. These need to be rectified if the manuscript needs to be published. The language needs to be corrected with the help of a native English speaker.

Response: We have corrected the English grammar.

References:

10. The references are not in line with the journal's instructions to authors. Please rectify this section. Please see https://bmccomplementalternmed.biomedcentral.com/submission-guidelines/preparing-your-manuscript/research-article

Response: We have corrected the references as per the instructions.

11. Reference 24 in the manuscript text is not in sequence.

Response: We now have corrected reference 24.