Reviewer's report

Title: Determinations of the effects of cinnamon bark fractions on Candida albicans and oral epithelial cells

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Reviewer: Victor Matsubara

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This manuscript investigated the impact of two natural products on C. albicans growth, biofilm formation, and adherence to epithelial cells. The toxicity, anti-inflammatory property, and the influence of these products on the epithelial barrier integrity were also tested using oral epithelial cell lines. Cinnulin did not reduce C. albicans growth but prevented C. albicans biofilm formation and attenuated its adherence to oral epithelial cells. In turn, Cinnamon bark oil had high antifungal activity and attenuated biofilm formation but was toxic at concentrations with anti-inflammatory capacity. Both cinnamon fractions reinforced the integrity of the oral epithelial barrier.

Comments:
- The abstract could show what MIC and MFC stand for, and its conclusion needs to be more objective.
- The manuscript does not explain how the two commercialised products were selected for this study. Perhaps previous studies testing the same products could be included in the background section.
- Overall the methods need to be better described to be reproducible:
  - Page 6 line 115 - Describe the number of dilutions/concentration of cinnamon fractions tested in the MIC assay.
  - Page 6 line 119 - Clarify the time intervals of OD recording over the 24h of incubation.
- It is not clear how a visual assessment was able to identify the inhibition of C. albicans growth, especially in a 96-well plate.
- Page 6 line 127 - How was the ratio established? Please add references?
- Page 8 line 154 - "24h"? Clarify how the Candida biofilm was grown in the biofilm viability test. Why was only cinnamon oil tested against mature biofilm?
- Page 8 line 171 - What was the concentration of each cinnamon fraction tested?
- In Table 1, why was the MFC/MIC Ratio for Cinnulin not calculated?
- The Membrane permeability assay tested only the effect of cinnamon oil on C. albicans. How about the other natural products?
- The effect of the natural products on both Candida biofilm formation and mature biofilm would be essential to draw a conclusion regarding the potential prophylactic and therapeutic effect of Cinnamon bark oil and Cinnulin. However, the later was not tested against 24h C. albicans biofilms. Consider the inclusion of this experiment in the manuscript.
- Page 16 line 352 - "These results suggest that Cinnulin PF® may be a promising anti-C. albicans agent because it specifically acts on biofilm formation but has no effect on growth."
  - Clarify why an effect on Candida growth is not desirable in an anti-Candida agent.
- The manuscript needs a stronger discussion section:
  - It is not clear why Cinnamaldehyde was tested in the study as there is not much discussion about the results of cinnamon bark oil and Cinnamaldehyde alone.
  - The authors need to bring a more in-depth analysis of the impact of these natural products on the host and pathogen. For instance, discuss the role of IL-6 and IL-8 in the immune system and how the change in the cytokine profile caused by Cinnamon products could influence the immune system against candidiasis.
  - The study could try to conclude which Cinnamon-based natural product would be better against C albicans considering their toxicity, antifungal, and anti-biofilm properties.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

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

Yes

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:

Acceptable

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