Reviewer’s report

Title: Susceptibility Testing of Leishmania spp. against Amphotericin B and Fluconazole using the Sensititre™ YeastOne™ YO9 Platform

Version: 0 Date: 05 May 2019

Reviewer: Surajit Bhattacharjee

Reviewer's report:

Kariyawasam et al investigated the use of the Sensititre™ YeastONE™ YO9 susceptibility plate for testing the susceptibility profiles of promastigotes of different Leishmania spp. They have determined the susceptibility profile of promastigote form of different Leishmania species against amphotericin B (AB) and fluconazole (FZ).

This study appears to be at its earliest stage for adopting the Sensititre™ YeastONE™ YO9 susceptibility plate as efficient and cost effective drug susceptibility checker against different species of Leishmania parasite. The work is preliminary and in the present form is of only a limited value.

Major Comments:

1. The major problem with the entire manuscript is the language (English is not up to the mark). Some of the sentences are excessively long, hard to follow and not easily understandable.

Few examples:

i. Page number 2, Line number 22 to 25 "Standardized clinically-approved drug ………….. a therapeutic agent a priori."

ii. Page number 2, Line number 25 to 29 "Our objective was to adapt the readily available ……………… … for the treatment of CL."

iii. Page number 3, Line number 43 to 46 "Given its current utility in ………………… concentration of the YeastONE Y09 plate.

iv. Page number 5, Line number 79 to 84 "Current clinical management ………………… ….. accessibility of the drug [3].

There are lot more throughout the manuscript.
2. There are several typographical mistakes and lack of uniformity throughout the manuscript.

Few examples:

i. Page number 2, Line number 39 and 40 the mean MIC values should be written as $\mu g/mL$ instead of $ug/mL$.

ii. Page number 6 line number 101 the unit for denoting the size of amastigote should be $2\mu m$ instead of $2um$.

iii. Page number 6 line number 111, 119 and 127, Sensistitre should be 'Sensititre'.

There are lot more throughout the manuscript.

3. From the manuscript it is appeared that authors investigated the use of Sensititre™ YeastONE™ YO9 susceptibility plate for testing the susceptibility profiles of promastigotes of different Leishmania spp.

But in majority sections of the manuscript they have focused on testing the potential utility of amphotericin B (AB) AB and Fluconazole (FZ) for the treatment of cutaneous leishmaniasis (CL). For example in page no. 3 line no. 25 to 29 the authors mentioned that "Our objective was to adapt the readily available Sensititre™ YeastONE YO9 plate used for routine antifungal susceptibility testing in yeast to determine drug susceptibility profiles in cultured isolates of Old World and New World isolates of Leishmania spp., in order to, as proof-of-concept, inform potential utility of AB and FZ for the treatment of CL".

Whereas, in the other sections of the manuscript they have generalized that "Customization of the plate may provide the opportunity to evaluate higher concentrations of FZ and an expanded panel of drugs with efficacy against Leishmania spp." It is better to include proper explanation in support of such generalized claims.

4. The authors are required to provide a comparative account in support of their claim that Sensititre™ YeastONE™ YO9 susceptibility plate is an efficient and cost effective drug susceptibility checker. They need to include the current techniques used in research laboratories for susceptibility testing and compare the result with the data obtained from Sensititre™ YeastONE™ YO9 susceptibility plate to prove its efficiency.
5. One of the major limitation of this study is the susceptibility checking of amastigote form of Leishmania parasite. The authors also mentioned that fact.

6. In the background section of the main manuscript the authors claimed that "In-vivo systems including animal models have been used extensively to determine Minimum Inhibitory Concentrations (MIC)s in Leishmania spp., however such systems could never be scaled to the clinical microbiology laboratory [14-18], and are therefore of limited utility." None of the references they have cited include information about in vivo testing of MIC against Leishmania.

7. The information given in the line no 105 to 110 "However, given that log-phase promastigotes are generally less susceptible to anti-Leishmania drugs than amastigotes [14-17], and detectable in a cell-free culture system incubated at room temperature, it has been proposed that promastigotes serve as a surrogate for determining the susceptibility patterns of isolates to pharmacotherapeutics independent of any cell-mediated parasiticidal mechanisms [14]." is not clear.

8. In the materials and method section (line number 163 and 164) authors mentioned "Concentrations of impregnated AB ranged from 0.12 µg/mL to 8 µg/mL, whereas FZ ranged from 0.12 µg/mL to 256 µg/mL [19]." But from the cited reference it not clear why they have chosen such concentration range in the present study.

9. In the discussion section an elaborate comparative analysis of the efficiency of Sensititre™ YeastONE™ YO9 susceptibility plate with other methods of susceptibility testing are need to be included to enrich the manuscript.

The manuscript is full of grammatical errors making it difficult to read. It requires a thorough editing upon revision.

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.

No

Are the conclusions drawn adequately supported by the data shown?
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