Reviewer's report

Title: In vivo activity of Sapindus saponaria against azole-susceptible and -resistant human vaginal Candida species.

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Reviewer: Francesca Mondello

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General

In this paper, Damke et al show that ethanol and butanol extracts of Sapindus saponaria pericarps inhibit in vitro and in vivo (rat vaginal infection model) Candida albicans and Candida glabrata. They assume low cytotoxicity of those plant extracts based on in vitro treatment of a cervical cell line, and include SEM picture of Candida-vaginal epithelium interaction.

This report adds to a long line of consistent evidence that several plant components exert anti-Candida activity. Though the mechanistic insight of these inhibitory properties are generally lacking, the above data are encouraging research aimed at integrating/replacing conventional antimycotics particularly with emerging fungal strains endowed with antibiotic resistance traits. Overall, these efforts are seen sympathetically. In this instance, however, there are several criticisms which require the Authors’ attention and possible revision of the scientific content of the paper and its presentation, as well.

Major comment

If I understand correctly the data presented on page 12 and Table 1, the anti-Candida activity of the extracts is exerted in vitro at very high concentrations, several orders of magnitude compared to active concentrations of antimycotics (i.e. mg/ml versus µg/ml). Under this situation, any comparison of activity is inappropriate and does not support potential in vivo applications. Qualifying as “excellent” (last line of page 12) an antifungal activity occurring in vitro at a concentration of 310 µg/ml (for C.albicans) and 620 µg/ml (for C.glabrata) is really senseless with the present antifungals activity standards. On the other hand, the quality of the in vivo data is hard to appreciate since apparently active concentrations are given as % and not as mg or µg/ml. The timeframe of in vivo results is limited to 21 days so that the readers cannot establish by themselves the persistence of the inhibitory activity. Finally, safety should be addressed (at least) by in-depth cytological analysis of the in vivo treatments not of a cell line. My opinion rests that, however safe, using an extract at those high concentration is not advisable and could never be competitive with antimycotics. The Authors should be encouraged to identify the active ingredient of the extracts as this may lead to a substantial improvement of the ratio antifungal activity/concentration, regardless of the fact that some irrelevant components of the extracts could also be detrimental.
Minor comments

1. The paper has many inconsistencies. The major one has already been mentioned above regarding concentrations. See also the MIC versus the CIM(?) and others throughout the text

2. The English usage requires in-depth revision. Some passages are terrible (see page 4, second paragraph; page 12, first line, under Plants and Components)

The SEM pictures do not add significantly to the scientific content of the paper and could be deleted.