Reviewer's report

Title: Anti-HIV-1 activity, protease inhibition and safety profile of extracts prepared from Rhus parviflora

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Reviewer: Raina Fichorova

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This manuscript by Modi and colleagues describes highly desirable functional properties of extracts derived from the plant Rhus parviflora rendering this natural product a promising anti-HIV microbicide candidate worth further in-depth investigation. The authors have performed a comprehensive investigation in accordance with currently accepted preclinical testing algorithms revealing favorable safety features including: lack of cytotoxicity to vaginal and digestive tract mucosal epithelial cells; morphologically preserved epithelial barrier and no upregulation of well-established proinflammatory cytokine markers in drug-treated mucosal cells; lack of damage to Lactobacillus species, which are an essential part of the natural mucosal barrier; anti-HIV activity in standard assays utilizing both reporter cell lines and PBMC, reduced HIV p24 production and suppressive HIV RT and protease activity in the absence of toxicity to the immune test cells. Moreover, the plant extracts appeared to stimulate Lactobacillus metabolic activity although a much more in depth analysis is required to determine if the candidate anti-HIV microbicide would stimulate lactobacillus growth and/or production of lactic acid and other beneficial metabolites. The suppressive effects on IL-8 and IL-1beta but not on IL-6 are interesting for a potential anti-inflammatory application and should be followed by further mechanistic analyses and animal evaluation. Topical anti-HIV microbicides with anti-inflammatory activities are sought as a dual HIV preventative modality. The study is logically designed; the manuscript is well written and shows an excellent understanding of the challenges facing the field of anti-HIV microbicide development.

No major compulsory revisions required

Minor essential revisions suggested:

Describe the statistical analysis method and show p values to evaluate significance of findings presented in figures and Table 2.

Level of interest: An article of outstanding merit and interest in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests:

No competing interests.