Reviewer's report

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

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**Reviewer:** Masahiko Kurokawa

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The authors examined the anti-HIV activity of extracts of Rhus parviflora using reporter gene based assays in TZM-b1 and CEM-GFP cells and cytotoxic assay by MTT. Also, p24 assays by ELISA were done to evaluate the inhibitory activity of the extracts in CEM-GFP cells and PBLs infected with HIV. The anti HIV activity was shown to be due to the inhibitory effect of HIV-1 protease activity by the extracts, but not that of RT activity. Furthermore, they examined the adverse effects on lactobacilli, epithelial monolayer integrity, and vaginal keratinocytes to evaluate the safety profile of extracts. The work presented herein may be a basis for describing the protective activity of extracts.

However, cytotoxicity is not properly evaluated in HIV-infected CEM-GFP cells or PBLs exposed to the extracts for 8 or 5 days, respectively, in p24 assays. In ELISA for the p24 assays, it is not shown that the extracts have no effect on the binding of p24 to antibody. The protective effect of extracts seems to be minimal in protease inhibitory assay. Therefore, the results presented can not be properly evaluated.

The authors used 2 types of extracts in this manuscript. They should describe the reason why they used 2 extracts and show their HPLC profiles to clarify the major components of the extracts and discuss the possibility of anti-HIV compounds included in extracts.

I think that the focus of this manuscript is unclear. Is the focus the anti-HIV activity of extracts or their clinical use? In safety assays of extracts, it seems that the authors focus on the prevention of sexual transmission of HIV. Is the extracts applied topically? If so, the authors should explain the rational reason why the topical use of anti-HIV agents including the extracts is effective and useful.

**Level of interest:** An article of insufficient interest to warrant publication in a scientific/medical journal

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** No, the manuscript does not need to be seen by a statistician.