Review of: "Toxicological evaluation of aqueous extracts of Clematis hirsuta and Rhamnus prinoides"

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Potential competing interests: No potential competing interests to declare.

This manuscript presents acute and subacute oral toxicity studies in rats to evaluate the safety of aqueous leaf extracts of Clematis hirsuta and aqueous root extracts of Rhamnus prinoides, two medicinal plants used in Kenya. A variety of parameters including animal weights, feed intake, hematology, clinical chemistry, and gross pathology were examined.

Overall, the study is well-designed and provides important preclinical toxicity data on these herbal extracts. Both the acute and subacute experiments seem to follow standard protocols and established guidelines. The results indicate no overt signs of toxicity up to the highest tested doses of 2000 mg/kg (acute) and 225 mg/kg (subacute) for each extract.

Major Strengths:

- Clearly describes the rationale and ethnobotanical background underlying selection of these two medicinal plants for safety studies. This provides helpful context.
- Provides details on plant collection, identification, extraction methods - this will allow reproducibility of the extracts.
- Both acute and subacute studies use relevant routes of administration, species, age, sample size, and dosing in line with toxicity testing guidelines.
- Multiple parameters assessed cover a wide range of potential toxicity manifestations.
- Statistical analyses seem appropriate - compares each treatment group to control using suitable tests.
- Overall, concludes the extracts appear relatively safe up to doses tested based on lack of adverse effects.

Weaknesses:

- Could consider including historical/anecdotal toxicity data on these plants or related species to put the findings in better perspective.
- Discussion is brief and does not sufficiently contextualize the findings among existing literature.
- Did not check for effects of extracts on organ histopathology - this could reveal microscopic changes even if gross pathology seems normal.
- Longer-term toxicity studies over months would provide fuller safety profile.
- Assessment of genotoxicity potential could be valuable.

In summary, this is a well-conducted study providing useful initial toxicity screening of C. hirsuta and R. prinoides extracts in rats. The results indicate relative safety up to tested doses. Some minor additions in discussion and study scope would

further strengthen the paper. Overall, the findings support continued investigation of the therapeutic potential of these plants.