

REVIEWER'S COMMENT:

There is a minor typographical error of "phychochemical" instead of "phytochemical" on page 3, line 4 perhaps. However, it is doubtful if the possible toxicity of the high doses of the ethanolic leaf extract of *Bergnia ciliata* with respect to the liver enzymes/renal function was highlighted in the revised manuscript. Most of the issues raised were adequately addressed. However, the possible toxicity of the high doses that was noted and raised in the original manuscript was probably not mentioned in the revision. Page 3, line 4 "phychochemical" "t" is missing, should be "phytochemical"

AUTHOR'S FEEDBACK:

- The typographical error "phychochemical" has been corrected to phytochemical.
- The doses (250mg/kg-1000mg/kg) of the extract were selected on the basis of the *in vivo* acute toxicity (LD50) of the extract, which was observed to be >5g/kg, which is the highest dose for acute toxicity testing in rodents (Lorke, 1983). The different doses were administered to assess the dose dependant effect of the extract on clearing malaria infection. The toxicity with respect to the liver enzymes/renal function of the host observed at higher doses of the extract can be due the effect of high drug pressure along with parasite infection. It has been observed in the present study that the low doses are not only effective in reducing the percent parasitaemia but are also safe to the liver and kidney function of the rodent host. Hence, it was concluded that the extract can be used as a phytomedicine against malaria infection even at the lower doses. Moreover, the phytomedicines are usually a combination of two or more herbal medications exhibiting synergistic action, so this plant can also be used one of the constituent of a polyherbal remedy where another constituent can ameliorate the toxic effect of the other.
- Also, most of the drugs used in clinical practice also exert many side effects (even at therapeutic doses) on the biochemical parameters of the host. The standard antimalarial chloroquine has also been reported to cause a significant increase in serum levels of hepatic (SGPT, SGOT, ALP, total bilirubin), renal (creatinine, urea) as well cardiac (creatine kinase-MB, C-reactive protein, malonic dialdehyde) function markers (El-Shishtawy *et al.*, 2015). The increased levels of the biomarkers return to normal over a period of time after the drug is metabolised and removed from the system.
- Moreover, in order to use this extract as a drug against malaria, further studies are being done to isolate, characterized and evaluate the *in vitro* and *in vivo* cytotoxicity and antimalarial activity of the active phytochemical present in the extract responsible for the observed activity.

References

Lorke D. 1983. A new approach to practical acute toxicity testing. Arch Toxicol 54: 275-287.
El Shishtawy MA, Hassan KH, Ramzy R, Berri F, Mortada M, Nasreddine S, Ezzedine M. 2015. Comparative toxicity study of chloroquine and hydroxychloroquine on adult albino rats. 1: 399-407.