Author's response to reviews

Title: Effects of kolaviron on hepatic oxidative stress in streptozotocin induced diabetes

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Title: Effects of kolaviron on hepatic oxidative stress in streptozotocin induced diabetes

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Author's response to reviewer:

May 27th, 2015
Editor,
BMC Complementary and Alternative Medicine

Dear Sir,

Please find attached the revised manuscript as per the comments of the reviewer. Answers to the reviewers’ comments are provided below. Please do not hesitate to contact us should you require further clarifications.

Sincerely Yours
Dr. O.R. Oyenihi (Nee Ayepola O.R.)
Reviewer 1

**Comment 1:** HPLC abbreviation is high performance liquid chromatography; however, the authors mentioned it as a High performance lipid peroxidation

**Response:** HPLC has been abbreviated as high performance liquid chromatography

**Comment 2:** In materials and methods section: the yield of kolaviron from ethylacetate extract was not reported.

**Response:** The yield of kolaviron has been reported in the manuscript.

**Comment 3:** Page no.4 line no 131, the volume of the sample (5 L), sodium phosphate (170L), and hydrogen peroxide (50 L) should be verified. Similarly in glutathione status analysis assay.

**Response:** The typographical error has been corrected and ‘L’ has been replaced with ‘µL’

**Comment 4:** Some abbreviations were not reported such as AAPH, DETAPAC

**Response:** Full meanings of abbreviated words have been included in the manuscript

**Comment 5:** The study can also take the support of histopathological analysis of liver tissues of experimental rats’ to confirm the hepatoprotective effect of KV in diabetic rats.

**Response:** Although histopathological analysis of liver tissues will provide additional information on the hepatoprotective effect of KV in diabetic rats, the present study has demonstrated the hepatoprotective effects of kolaviron through reduction of hepatic oxidative stress and apoptotic index.

**Comment 6:** Hepatic injury biomarkers was not reported
Response: Biomarkers of Hepatic injury were not reported in the present study because it was reported in our previous study (BMC Complementary and Alternative Medicine, 13:363 – 371).
**Reviewer 2**

**Comment 1:** It has been shown that SOD activity increases in the C+KV group. This could be since KV activates SOD or it could be since the drug is toxic and that leads to an increase in SOD. Further analysis of this need to be carried out. Also the significance of C+KV group has not been mentioned.

**Response:** Superoxide dismutase (SOD) is an important antioxidant defence in living cells that catalyse the breakdown of superoxide radical anion. The increase activity of SOD in rats accompanied by an increase in oxygen radical absorbing capacity (ORAC) after kolaviron treatment might be a mechanism to boost antioxidant defence. In addition there is a report of increased mRNA expression of SOD in cultured interstitial Leydig cells (ILCs) in the presence of kolaviron (Abarikwu et al., 2012). The antioxidant and tissue protective effects of kolaviron have been reported (Adedara & Farombi, 2013; Ayepola et al., 2013). In the present study, the level of malondialdehyde (a lipid peroxidation biomarker), and apoptotic index did not increase significantly in ‘C + KV’ group in comparison to ‘C’ group further supporting the non-toxic effects of kolaviron in the present study.

The C+ KV group was included to observe the effect of kolaviron in control (normal) rats. The potentials of kolaviron to increase SOD activity and oxygen radical absorbing capacity (ORAC) were observed in C+ KV group in comparison to C group.

**Comment 2:** Abstract: Line 21: It should be High-performance liquid chromatography (HPLC) instead of High performance lipid peroxidation.

**Response:** HPLC has been abbreviated as high performance liquid chromatography

**Comment 3:** Drug is dissolved in DMSO is mentioned in study design, but the concentration of DMSO is not mentioned which is very important. Why is DMSO used in in-vivo study? You can suspend or make emulsion of kolaviron using CMC or tween 80.

**Response:** Dimethyl sulfoxide (DMSO) is a solvent for organic and inorganic substances. DMSO was used as a vehicle for kolaviron because of its complete dissolution in the solvent.
Kolaviron (100mg/kg) was dissolved in DMSO to a final concentration of 70 mg/ml. DMSO has been used as a vehicle in similar studies:


**Comments 4:** Mention full form of DETAPAC.

**Response:** Full meanings of abbreviated words have been included in the manuscript.