Author's response to reviews

Title: In Vitro Antibacterial and Antibiotic-potentiation Activities of the Methanol Extracts from Beilschmiedia acuta, Clausena anisata, Newbouldia laevis and Polyscias fulva against Multidrug-Resistant Gram-Negative Bacteria

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Author's response to reviews: see over
Dear Editor, Dear Tom,

Thanks for sending the reviewer’s recommendations for the above manuscript. We are now resubmitting the revised version taking in account their recommendations to improve it. The revision made are highlighted in recolor color in the manuscript and also listed point-by-point below.

I hope you will found the work suitable for publication now

best regards

(Prof. Dr. Victor Kuete)

**Reviewer#1: William Schwan**

**Reviewer’s report:**

**Major Compulsory Revisions**

1. Several sentences are poorly worded.

   **Answers:** The manuscript has been thoroughly check for grammar and language editing

2. The background information should have a better transition between the first and second paragraphs. Furthermore, the authors should at least reference the discovery of antimicrobials from some of the plants that were used in the study.

   **Answers:** The transition sentence was improved and references to the antimicrobial use of the plants were provided

3. Somewhere the authors should have a table showing the MIC values of their strains against tetracycline, ciprofloxacin, chloramphenicol, ampicillin, and kanamycin as a frame of reference. This table would provide a foundation for their synergy experiments.

   **Answers:** all these values are available in Tables 5 and 6; see column extract and concentrations (for concentration 0 we have the MIC for antibiotic alone)

4. Any MIC values above 256 ug/ml should be listed as > 256 ug/ml and considered as negative values for interpretation. A drug company is not going to be interested in pursuing those extracts with MICs > 256 ug/ml.

   **Answers:** we agree with the reviewer; However, the cutoff points are clearly provided in the discussion section. This was the case with antibiotics. For extracts, we maintained values up to 1024 µg/mL because the classification of activity are different and its helps appreciating the antibacterial spectra of the tested plants.
5. No additional processing of the samples beyond crude extracts was attempted.

*Answers: This is limitation of our study; the purification of the best extract will be further performed: this has now been added to our conclusions.*

Minor Essential Revisions
1. There are several misspellings in the paper.

*Answers: the manuscript was thoroughly checked and corrected.*

**Reviewer#2: Prasanta K. Bag**

**Reviewer’s report:**

The present manuscript demonstrated the antibacterial activities of Beilschmedia acuta, Clausena anisata, Newbouldia laevis and Polyscias fulva. Their synergistic effects with reference antibiotics against MDR strains of Gram-negative bacteria also have been evaluated. However, antibacterial activities of Beilschmedia acuta, Clausena anisata and Newbouldia laevis and antifungal activity of Polyscias fulva have been previously reported.


*Answer: This is wright, but the activity was not carried out on resistant bacteria: Related information were reported in table 2.*


*Answer: These authors used Beilschmedia obscura not Beilschemidia acuta tested in this work*


*Answer: These authors tested the antifungal not antibacterial activity of Ploysccia fulva.*

Although antimicrobial activities of these plants have been previously reported,
results obtained especially for synergistic activity in the present study are interesting.

**Answer: Thank for this appreciation**

Comments:
1. Abstract. Plant’s full scientific name including family name must be indicated. “71.1% of the bacterial strains for *N. laevis* ---, 43.3% for *C. anisata* leaves extract, 50% and 36.5% ---.” Since only 26 strains were used, percentage of bacterial strains should be within first bracket after indication of exact number of bacterial strains giving positive results.

**Answer: corrections have been done as requested**

2. Why these plants were chosen for this study that should be justified in the introduction section.

**Answer: done**

3. Page 3. Lines 68-. “The present work was therefore designed to investigate the antibacterial potential of four Cameroonian medicinal plants used traditionally in the treatment of bacterial infections, namely Beilschmiedia acuta Kosterm (Lauraceae),---.” References for traditional use in bacterial infections must be given.

**Answer: this has now been provided at the end of the introduction section**

4. Since antimicrobial activities of the selected plants have been previously reported, the authors should focus on the synergistic activities of these plants’ extract in conclusion section for Abstract and the text, and in ‘Aim’ section of the ‘Introduction’ (main text).

**Answer: The antibacterial activity of the plant was not tested against multidrug resistant (MDR) bacteria. One of the aim of this work was to assess the ability of the tested plant to fight MDR bacteria.**

5. Page 8, lines 178-179. Since the antimicrobial activity of these plants has been previously reported, Delete the lines “To the best of our knowledge, the antibacterial activity of the studied plant extracts towards MDR bacteria is being reported herein for the first time.”

**Answer: done**

6. Phytochemical data for these plants’ extracts must be shown.

**Answer: Data on the phytochemistry of the tested plants are shown in Table 2, Column 5 (Bioactive or potentially active compounds isolated from plant)**

7. Toxicity test for these extract must be done.

**Answer: There is no possibility for us to perform any toxicity test on these samples. Nevertheless, we previously demonstrated the low cytotoxicity from *Polyscias fulva* as well as from *Beilschmiedia acuta* on normal AML12 hepatocytes. This information has been added in the discussion section**

8. Some syntax error through out the MS must be corrected.
Answer: syntax error were corrected throughout the text