Review Form 3

Journal Name:	**Journal of Complementary and Alternative Medical Research**
Manuscript Number:	**Ms_JOCAMR_122990**
Title of the Manuscript:	**Moringa oleifera supplement for HIV/AIDS patients is safe but does not influence the CD4+ and CD8+ t-cell patterns**
Type of the Article	**Original Research Article**

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PART 1: Review Comments

Compulsory REVISION comments	**Reviewer's comment**	**Author's Feedback** *(Please correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Please write a few sentences regarding the importance of this manuscript for the scientific community. Why do you like (or dislike) this manuscript? A minimum of 3-4 sentences may be required for this part.	**This Manuscript is importance to the Scientific Community as It provides cheaper, cost-effective, non-toxic, natural alternative** *M. Oleifera* **to the not only costly, but also toxic ARVs. Generally, I like the Manuscript because of the Following;** **1. It involves Humans, Real HIV Infection Patients who are on ARV treatment.** **2. It uses an Interventional/Experimental Design (Albeit, Quasi-Experiment), with an Intervention and Evaluation of the Impact of the Intervention in the same study.** **3. The ability of the Design Used to establish Causal Association between Variables, when time is a Priority.** **4. Among the very first and few studies to investigate the effect of *M. Oleifera* supplementation on CD8+T cells in Humans and HIV Infection**	
Is the title of the article suitable? **(If not please suggest an alternative title)**	**Although the Title is Suitable for the Article, it is Deceiving and Need to be Revised to Reflect the True Findings of the Study.** **My suggestion is to Revise it to** *"Moringa Oleifera supplement for HIV-infected patients is safe and may significantly influence the CD4+ T-cell patterns"*	

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Is the abstract of the article comprehensive? Do you suggest the addition (or deletion) of some points in this section? Please write your suggestions here.	**Though the Abstract is Adequate, it is NOT comprehensive enough, to make it an "Informative Summary" of the Document.** **My Suggestion is to consider including the following;** **1. The main objective of the study** **2. In the Methodology Section to Include the Total Numbers for the Intervention/Treatment group (n = 99) and for the Control Group (n= 74), the actual interventions for the two Study Grous e.g. To the Intervention group, 8 grams twice/day (4 grams in the morning and 4 grams in the evening), for the entire 6 months of the study.** *3.* **The Primary end points for the study and how the measures were evaluated done. E.g**. *"The primary end point for this study were safety and effect/impact or influence of the M. Oleifera Supplementation on CD4+ and CD8+ T cell patterns. The Baseline measures of the CD4+ and CD8+ T cells and Glomerular Filtration Rates for the two study groups were evaluated at the beginning of the study and thereafter, reassessment of the same measures done, at the third and at 6 months The baseline measures and the subsequent ones at the third and 6th month were analysed and compared for any variations".* **4. To include in the Methodology, the Methods of Data Collection used e.g. Acquisition from Analyzer/Computer printouts Reports, questionnaires or Interviews, Analysis Software/Application Used e.g. SPSS or MS-Excell, Tye of Analysis e.g. Descriptive Analysis for Means± Standard Deviation, ANOVA for Group Differences/Variations and paired t test for Repeated Measures.** **5. Revising of the Results section to reflect the Truth as Presented in Tables 2 and 3. According to Table 2,** *"There was not only a quantitative change in values, but also a statistically significant Differences/Variations in CD4+T cell Counts at Third and 6th Month from the Baseline Measures for Both the Intervention/Treatment (P= 0.002) and Control Grous (P= 0.001)". There was also quantitative Changes in the CD4+ T cells from (1075 to 1079 for the Intervention and 1058 to 1070 for the Controls), although it was not Statistically Significant (P=0.994 and P=0.954, respectively)".* **N.B: The Absence of the Evidence Does Not Mean Lack of Evidence. Lack of Statistical Significance for CD8+ T cells, Does Not Mean There Was No Change in the Cell Counts, it only Means the Change Observed Could be Merely Due to Chance or Random Error".** **6. Not focusing primarily on the Statistically Nonsignificant results of Table 3, But Focus on the Statistically Significant Changes of CD4+ T cells for both the Study Grous in Table 2, and the ANOVA F value also for the CD4+ T cells in the two group that is also, that indicates the "Between-the-groups", more specifically differences occasioned by segmentation with M. Oleifera, as the main source of variations observed, assuming the only major differences apart from the age and gender, was in the "Intervention" given.** **7. Revising the Conclusion of the Abstract, Based on Numbers 5 and 6 above.**	
Are subsections and structure of the manuscript appropriate?	**The Subsections and Structuring of the Manuscript are appropriate.**	
Please write a few sentences regarding the scientific correctness of this manuscript. Why do you think that this manuscript is scientifically robust and technically sound? A minimum of 3-4 sentences may be required for this part.	**The choice of Experimental/Interventional Design of quasi-experimental of Regression Discontinuity, Integration of an Intervention and an Evaluation Phases in the same study design, Use of Scientific Criteria and Guidelines such as CONSORT FLOW 2010 for reporting Interventional Studies to Draw Flow Diagram of the Participants, Makes the Manuscript Not only Scientifically Correct, but also Technically Sound.** **Likewise, the use of Laboratory-based assaying of CD4+ and CD8+ T cells Using Flow Cytometry and Automated Chemistry Analyzer for measurements of Creatinine and Use of a Recognized Formula Cock Croft Gault formula (CGF) adds to the Technical Soundness of the Manuscript.**	
Are the references sufficient and recent? If you have suggestions of additional references, please mention them in the review form.	**The References are Not only Sufficient but also Recent.**	

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Minor REVISION comments **Is the language/English quality of the article suitable for scholarly communications?**	The Language and English Quality Is Suitable for Scholarly Communication	
Optional/General comments	Some of the Optional Comments include; • Addition of the Word Infection to "HIV" in the opening sentence of the Abstract. • Moving all Statements Describing Tables and Figures from the Top to the Bottom of the Tables and Figures. • Sections 2.1 and 2.2 Contradicts each Other On the Frequency of Reassessments (Monthly or a 3 different time points), which need to be addressed. • Consider adding the Hypothesized Mean Difference for the Unpaired t test. • Given the Observational and nonrandomization nature of quasi experimental studies and associated Limitations of potential Confounding and Selection Bias, and that Factors such as the Age and Gender are Known Confounders, Consider Either; Stratified Analysis by Gender and by the Age-specific Categories, or adjustments for the same at the analysis. ***N.B: In the absence of these, consider adding Limitations to the Study at the end of Discussion Section and the Need for Cautious Interpretation of the Results and recommendation of further Investigations using more Robust Designs e.g. RCTs to confirm the observed Findings.*** • Consider the following Statements in the Revision of the Description of Table 2; *"Though there were some quantitative changes or increases in the CD8+ T cells count at month six from the baseline levels, the changes were not statistically significant. The ANOVA F value for CD4+ T cells in Both the intervention groups (6.2863) and Control Group (6.8949) that is relatively high and too far from "1" or the "point of no variation", is important for this study. Fundamentally, it implies that the "between-groups" variance was larger than the "within-groups" variance. Therefore, the between-groups variance, that is changes occasioned by supplementation in one group but not in the other, was the main source of the variation observed. Consequently, the statistically significant differences in CD4+ T cell counts observed in the two study groups can be associated to the supplementation and not to the ARVs both groups were taking".* • Consider the Following Statement in the Revision of Description of Table 3; *"Although the mean CD4+ T cell count of the intervention group was higher (656.23 ± 274.8) than that of the control group (624.53 ± 299.32) in the sixth month of the study, the rate of change in cell counts between the two groups was not statistically different. There was no significant difference in the rate of change in the cells count as indicated by the P values for the means of CD4+ T cell counts and CD8+ T cell counts in month three, as well asCD4+ T cell counts and CD8+ T cell counts in month six between the two groups (p <0.005)".* • To identify clearly actual Dosage of Studies cited Duration of Intervention (Of How Many Grams and for how wrong?) caused immunosuppression [21]. • To establish clearly what Constitutes Low Dose and High Dose for M Oleifera, and Compare with the current Study's Dosage of 8gms//day. • Consider the Following Statement in the Discussion of Contradicting Findings; *"These contradictory findings from the current study could be explained by the differences in the designs and sample sizes, as well as the heterogeneity of the study participants used. While the current study was a quasi-experimental study, that does not involve randomization of participants, the aforementioned studies were double and single-blinded randomized controlled trials".* • To Consider the following Statement in the Discussion of Contradicting Findings on CD8+ T cells; *"A plausible explanation for these contradictory findings is that all the studies were with animal models"* • To Consider Including Different Referencing Styles inside the Text such as In Text Referencing; *"In a randomized controlled trial/study conducted by Novitra et al. (2020)……."*	

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PART 2:

	Reviewer's comment	**Author's comment** *(if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)*
Are there ethical issues in this manuscript?	*(If yes, Kindly please write down the ethical issues here in details)*	

Reviewer Details:

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