

Point-to-Point Response Letter

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Authors	Diptasree Mukherjee, Arunkumar Krishnan

Round 1

Reviewer #1

1. **This review summarized the molecular pathways involved in oral carcinoma and explores different therapeutic interactions of curcumin and the role of nanocurcumin formulations in oral cancer, and this might be useful for head neck surgeons and researchers focusing on this area.”**

Response: We thank the reviewer for taking the time to review our manuscript. We appreciate your time and for sharing the favourable comments. We have changed the manuscript title to “Therapeutic Potential of Curcumin and Its Nanoformulations for Treating Oral Cancer” because we have revised and included the latest updates about Nanoformulations based on the recent advanced in this field. This review is more comprehensive and detailed. We believe that the present version of the manuscript is comprehensive and detailed, which would help clinicians and researchers understand and learn the importance of curcumin and the gap in knowledge on this topic.

Reviewer #2

We thank the reviewer for taking the time to review our manuscript and sharing your comments. We appreciate your time. We have revised the manuscript and supplementary and improved the manuscript as recommended. We have changed the manuscript title to “Therapeutic Potential of Curcumin and Its Nanoformulations for Treating Oral Cancer” because we have revised and included the latest updates about Nanoformulations based on the recent advanced in this field. This review is more comprehensive and detailed. We believe that the present version of the manuscript is comprehensive and detailed, which would help clinicians and researchers understand and learn the importance of curcumin and the gap in knowledge on this topic.

- 1. Are there controversies in this field? What are the most recent and important achievements in the field? In my opinion, answers to these questions should be emphasized. Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript.”**

Response: Thank you for your recommendation. We have revised the entire manuscript, discussed the recent achievements, and highlighted important key points based on the current literature.

We have included a new section with the heading “Properties of curcumin” and future directions with conclusions as the important requirement to be addressed in future studies to understand curcumin's adjuvant effect in cancer treatment for clinical use.

- 2. The results and discussion section is very weak and no emphasis is given on the discussion of the results like why certain effects are coming in to existence and what could be the possible reason behind them?”**

Response: This review article didn't include any subsection as results or discussion. However, we have included the main section and subsections to explain the pathophysiology of cancer, curcumin's critical adjuvant effect, and curcumin's impact on other anticancer agents.

In addition, the effects of various novel formulations of curcumin are discussed in detail, and the importance of these preparations is compared with the help of the latest literature. We have included the recent studies that included and discussed under the heading “Novel formulations of curcumin in oral cancer treatment.”

3. Conclusion: not properly written.”

Response: We improved the conclusion section. Furthermore, we have divided and rewritten the conclusion as “Challenges and future direction” to highlight the points where future studies are required to understand curcumin’s impact and the practical challenges of using curcumin in clinical practice. Hence, we believe this section would help clinicians and researchers understand and learn the importance of curcumin and the gap in knowledge on this topic.

4. Results and conclusion: The section devoted to explaining the results suffers from the same problems revealed so far. Your storyline in the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from what one can infer from the empirical results.”

Response: As mentioned earlier, we didn’t include any subsection as results or discussion in this review article. However, we understand your concern about improving the manuscript to support the conclusions. Hence, we have included various sections to understand the properties and effects of curcumin and subsections. Furthermore, the sections with headings “Properties of Curcumin,” “Effect of curcumin in oral cancer” (previously “Role of curcumin in oral cancer treatment”), “Clinical trials using curcumin for oral lesions,” “Novel formulations of curcumin in oral cancer treatment” (previously included “Nanoformulations of curcumin” and “Nanocurcumin in oral cancer”) and “Challenges and future directions” (previously had “Challenges and future directions” and “Conclusion”) are divided as a key subsection to improve the language, better readability and enhance the understanding of the readers. Notably, the current “Challenges and future directions” contain a conclusion at the end with statements reflecting on the findings of the studies described in the review.

5. The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning. A real discussion should also link the findings of the study to theory and/or literature.”

Response: We improved the manuscript with the help of recent studies relating to curcumin's application in oral cancer. We have rewritten the various sections of the manuscript. We have organized them with subsections by exposure to gain a better understanding of the limitations of the evidence and clinical research in curcumin to treat cancer.

In summary, we have rewritten the manuscript to review recent progress in molecular pathways involved in oral carcinoma and to explore different therapeutic interactions of curcumin and the role of novel curcumin formulations in oral cancer.

Overall, the paper summarizes the current state of knowledge on the topic. It creates an understanding of the role of curcumin in oral cancer for the reader by discussing the findings presented and comparing them based on recent literature.

6. Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly. I found so many typos throughout the manuscript.”

Response: Thank you for pointing that out. We have improved the language of this manuscript by doing multiple revisions and meticulous proofreading to improve the language and for better readability.

7. English is modest. Therefore, the authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.”

Response: We have improved the language of this manuscript by doing multiple revisions. In addition, we have performed meticulous proofreading to improve the language to grade the “A” standard and for better readability.

Round 2

Specific Comments To Authors: The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning. A real discussion should also link the findings of the study to theory and/or literature.