

Review of: "[Review Article] Green Strategies for the Synthesis of Quinolone Derivatives"

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Potential competing interests: No potential competing interests to declare.

[Review Report of P5M2Z8: Qeios]

The manuscript entitled "Green Strategies for the Synthesis of Quinolone Derivatives" is a summary of the recent advancements in green chemistry methods for establishing quinolone scaffolds to develop non-toxic and eco-friendly techniques for the synthesis and development of novel drugs. Even though the subject is quite interesting, in my opinion, there are many weak points throughout the manuscript. So, according to me, many points deserve further attention from the authors, and I therefore would only recommend publication in *Qeios* after major revision.

1. The graphical abstract is not appealing. Revise it by considering only the main aspects.
2. The authors should mention why they have selected quinolone derivatives for review.
3. What is the time duration for which the review covers? It should be mentioned in the introduction and also in the abstract.
4. In the introduction, compare the overall bioactivity profile of the quinolone moiety with that of other heterocyclic compounds, discussing drug resistance and bioactivities. The following papers are suggested to be included, discussed, and cited;
 - <https://doi.org/10.1080/14756366.2016.1238363>
 - <https://doi.org/10.1016/j.saa.2017.09.019>
 - <https://doi.org/10.1007/s00044-012-0388-0>
 - <https://doi.org/10.1002/aoc.6054>
 - <https://doi.org/10.1007/s11696-022-02123-1>
 - <https://doi.org/10.17344/acsi.2021.7182>
 - <http://dx.doi.org/10.17576/jsm-2020-4908-11>
5. Authors should focus on the green synthesis of quinolone derivatives as the title. Authors should write about the new green strategies for the preparation of quinolones.
6. Add a timeline figure showing the progress of the field.
7. The yield must be discussed to clarify the benefits of using green catalysts.

8. The article is not deep enough and needs further discussion by the authors. The manuscript lacks depth and focus on the subject areas. It seems that the authors have just collected the results and summarized them in a single file. However, the data is not well structured and is without any technical discussion.

9. There is also a deficiency of critical analysis of all data published about this theme and, as a summary/conclusion, a discussion about SAR pointing out the most promising drugs of this type concerning – future perspectives – and the benefits/advantages of discussed green strategies and quinolone derivatives relative to many other drugs under study and in the market.

10. Although this is a review, being quantitative is important. The authors must explain why the given compounds are more active among the series. Were these extremely positive results? What is the reason behind their activity? Is there any structural difference, or any kind of other factor? This should be clarified in the revised manuscript. Consider and cite the following review papers;

- <https://doi.org/10.1016/j.molstruc.2022.133044>
- <https://doi.org/10.1016/j.molstruc.2023.135744>
- <https://doi.org/10.1080/00958972.2023.2208260>

11. What about the mechanism of their bioactivities? Are they different from already available drugs in terms of their mechanism of action? This will be the key information.

12. Draw all the structures/schemes with proper bond lengths and angles. Mention all the substitutions in the figures.

13. The presentation should be more attractive to the reader. In my opinion, the manuscript needs a reorganization and should be re-structured and also complemented with more scientific/experimental information from literature data. Add more interesting figures. Not only the presentation of the structures of the compounds but also spectroscopic data supporting those structures. Reference the biochemical/biological assays/methods used to evaluate the biological properties of the compounds and their results and significance.

14. The figures' resolution is very low and necessary to improve all the figures in the revised manuscript. Also, the figures look to be squeezed or elongated unproportionally. Authors need to revise the figures following standard ways. Improve figure 5.

15. Use the same font style and size throughout the manuscript, including schemes/structures, figures, and their captions.