Review of: "Synthesis and Antibacterial Screening of Cefradine Schiff Bases and Their Metal Salts"

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Potential competing interests: No potential competing interests to declare.

Dear editor

Thank you Qeios, for the invitation to review this manuscript.

The article entitled “Synthesis and Antibacterial Screening of Cefradine Schiff Bases and Their Metal Salts” contains two parts, the first on the synthesis and characterizations of the antibiotic cefradine based molecules of the first generation of cephalosporins and the second part, which concerns their antibacterial potential.

In my opinion, this article needs more explanations. To improve the quality of the manuscript, the following corrections should be made:

1. Keywords

- Must specify the key words.

2. General procedure for the preparation of Schiff bases of cefradine (3-8)

- There are no data for **compound 3** ?

3. Spectrophotometry data and characterization

- IR and NMR spectra appear sufficient to confirm chemical structures.
- However, to strengthen the NMR/IR data. Include full spectrum and add other analysis (e.g. mass spectrometry, UV…).

4. Biological Activity

- Only two bacterial strains have been studied.
- Why choose *Staphylococcus aureus* and *Escherichia coli*?
- Please mention the ATTC number for *Staphylococcus aureus* and *Escherichia coli*.
- Insert the concentration(s) used.
- From the antibacterial activity test, I notice that these structural modifications do not show any improvement compared to cefradine. The most active compound 23 has an inhibition zone of 18mm and 17mm against *E. coli* and *S. aureus* respectively. Based on this data, activities described as “good” appear to be overestimated. And please include the citation.

- Determine MIC and MBC, and deduce the bactericidal or bacteriostatic mode of action.
- Please broaden the spectrum of activity by testing other Gram + and Gram – strains.
- Please show the structure activity relationship
- To better, understand the type of interaction between active derivatives and bacteria. Please add the theoretical study "molecular docking as an example)

5. Reference

- Please update references.

In conclusion

For cephalosporin's there are 4 generations, I propose to make syntheses based on the fourth generation molecules, and to establish other biological activities such as antibacterial against several bacteria, antioxidant, antifungal, anti-inflammatory....

In this manuscript, the chemistry is acceptable, but from the perspective of developing new antibiotics, the biological activity is marginal and poorly performed and requires a lot of work.

Therefore, in my opinion, this manuscript is not ready in its current form and will require the authors to resubmit it.