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.

Spectrophotometry Data & Characterization

- The IR and NMR spectra seem sufficient to confirm chemical structures. However, including full spectra in supplementary data rather than just selected peaks could strengthen the characterization.
- No mass spectrometry data is provided to complement the NMR/IR data. Adding LC-MS or HRMS analysis would further verify composition and purity.

Toxicity Testing

- No toxicity assays were performed. Assessing cell viability/cytotoxicity is an essential component when evaluating potential new antibiotic leads prior to claims about their promise.

Antibacterial Activity

- The activities of the new compounds are generally less or equal to the cefradine standard. The most active compound 23 has activity comparable to cefradine against E. coli, but weaker inhibition of S. aureus. Based on the data, the described "good" or "best" activities seem to be overstatements given their inferior profiles.
- No information on mode of action, resistance potential, or selectivity is provided. The clinical relevance compared to existing antibiotics is unclear.

Overall Significance

- While a modest inhibition by select derivatives is demonstrated, the authors overreach in positioning this incremental modification of cefradine as significant prior to further testing in cellular and animal infection models. The microbiological data does not yet support claims of enhanced activity.

In conclusion, the chemistry seems sound but the biological activity is marginal and characterized inadequately from a drug development perspective. Significantly more testing is required to substantiate any superiority over established antibacterial agents against these strains.strains. There are several areas requiring significant additional experimentation and data analysis before the claims about the biological activity would be suitable for publication:

Recommendations for Publication:

1. Conduct cytotoxicity assays using mammalian cell lines to demonstrate the compounds are non-toxic or have acceptable therapeutic indices. This is standard practice in early stage antibiotic drug discovery.
2. Compare the activity of the most potent derivatives head-to-head against the cefradine parent in dose response analyses spanning a concentration range. The single high concentration testing does not adequately reveal if efficacy, potency, or spectrum is improved.
3. Profile the antibacterial kinetics and mechanism of action. For example, analyze outer membrane/cell wall disruption, protein, DNA or RNA synthesis inhibition. This could provide insight into the mode of action.
4. Test against a more extensive panel of bacterial strains, including clinical isolates with characterized resistance mechanisms. Lack of inhibition on resistant strains would demonstrate these offer no clear advantage.
5. Eliminate claims around the compounds as "good", "best" or having "enhanced" activity until rigorously demonstrated via proper statistical analyses in repeatable experiments encompassing multiple strains.

In summary, while I cannot recommend publication now, the above 5 recommendations would significantly strengthen the biological activity assessment. If the authors can demonstrate even one or two derivatives with clear, statistically significant improvements in potency or spectrum compared to cefradine, it may warrant publication after appropriate revision.