

# Review of: "Inhibition Success of a Virtually Created Molecule: Pseudoeriocitrin and Femtomolar Inhibition"

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**Potential competing interests:** No potential competing interests to declare.

## Critique:

This work seems nice on many grounds but lacks rigorous bases for consideration as a comprehensive resource with potential for future scientific impact. The reasons are briefly as follows:

1. "alternative treatments to replace synthetic drugs." This is vague and uninformed. In my opinion, the motive to replace "synthetic drugs" is not possible. Molecules that become drugs are synthesized by natural systems including humans. Those synthesized by plants are not available in high quantities to meet the demands of clinical use, hence have to be scaled up through chemical synthesis. Chemical synthesis can be de-novo or semi-synthesis.
2. *Syphacia obvelata* rarely infects humans, according to the CDC in 2019 (<https://www.cdc.gov/dpdx/enterobiasis/index.html>). Also, as a parasite in rodents, it is important to ensure that their populations are regulated. However, their presence in the gut provides some immunomodulatory effects against inflammation. The authors did not provide a valid scientific basis for targeting the proteins of this parasite; hitherto, a basis for targeting the parasite itself.
3. Performing protein-ligand docking is not the initial step towards the development of new drugs. Establishing a basis for the etiology of a disease, understanding the biochemical pathways involved in the onset, progression, and symptomatic or asymptomatic features of a disease, is the probable starting point.
4. Authors should review the downstream effects of targeting COX proteins in order to validate a comprehensive list of protein targets. Authors claim to be in search of drugs with minimal side effects; however, if this pseudo-natural product molecule is targeting COX proteins in humans, the side effects can be enormous (<https://www.ncbi.nlm.nih.gov/books/NBK549795/#:~:text=Adverse%20effects%20vary%20depending%20on%20the%20COX%20inhibitor%20used.&text=Upper%20GI%20side%20effects%20get,u>).
5. Molecular dynamics simulations should be carried out to assess the stability of the docked complexes, and possibly the kinetic rates.

## Comments:

The above critique provides insightful observations regarding the work's strengths and areas for improvement. However, it would benefit from clearer organization and more specific suggestions for enhancement. Below are some suggested revisions:

1. The statement regarding "alternative treatments to replace synthetic drugs" lacks clarity and depth. Consider elaborating on the challenges associated with replacing synthetic drugs with natural alternatives, such as issues related to scalability and availability.
2. The discussion on *Syphacia obvelata* infection in humans could be expanded to provide a more comprehensive understanding of its relevance to the study. Additionally, incorporating recent research findings or epidemiological data may strengthen the argument regarding the significance of targeting proteins from this parasite.
3. Highlighting the importance of establishing the etiology of a disease and understanding biochemical pathways before proceeding to protein-ligand docking is a valid point. It would be helpful to provide specific examples or references to support this claim and guide future research directions.
4. The suggestion to review the downstream effects of targeting COX proteins is valuable for ensuring a comprehensive assessment of potential drug candidates. Including relevant literature or case studies illustrating the consequences of COX protein inhibition could reinforce this argument.
5. Emphasizing the potential side effects of targeting COX proteins with pseudo-natural product molecules underscores the importance of thorough evaluation and risk assessment in drug development. Providing specific examples or hypothetical scenarios illustrating these potential side effects would enhance the persuasiveness of this argument.

Overall, by refining the organization and providing more specific examples or references to support the critiques, this commentary can offer valuable insights for further improving the research and its potential impact in the field.