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

Giselle A. Borges e Soares[1]

1 University of Toledo

Potential competing interests: No potential competing interests to declare.

The article is very interesting, but I believe it requires more experimental work to be performed to be considered for publication. It has several grammatical errors that need to be corrected as well. Scientifically speaking, I would like the following comments addressed as I believe they will improve the impact of the work.

1. In the introduction, it would be best to provide more up-to-date statistics/demographics. Data from 2012 is cited, which is more than 10 years old.
2. In the introduction, the rationale as to why novel anthelmintics need to be developed needs more justification. “Therefore, the discovery of new anthelmintics with fewer side effects is a very important and challenging task”. What are the common side effects, and why do these side effects occur? Why do new anthelmintics need to be developed? What are the drawbacks of the already existing anthelmintics?
3. Please rephrase this sentence as it is very confusing and complex “Because the unknown genome sequence and the lack of crystallized structure of the proteins belonged to *Syphacia obvelata*, homology models of mitochondrial cytochrome c oxidase (COX) proteins can be useful for *in silico* docking experiments in order to investigate the antinematodal properties of some drug candidates against *S. obvelata”* Also, correct the grammar.
4. Please describe the significance of docking studies and justify/provide a reference for this statement “Protein-ligand docking simulations performed by *in silico* molecular modeling are the first step towards drug development efforts, providing researchers with atomic-level data on target-drug interactions. Such computational experiments are of great importance in reducing the workload around drug development efforts”.
5. Have the structure of eriocitrin and pseudoeriocitrin in the introduction so that readers can compare the structural differences at a glance. Also, improve Figure 1. Possibly use ChemDraw.
6. Please rephrase this sentence “Before one molecule showed anomalous binding in the docking studies, we retrieved the PDB file of this molecule from the FooDB database ((www.foodb.ca)) in November 2019 (ligand ID: FDB016547)”. Which “one molecule” are the authors referring to?
7. Please rephrase “Its fact that radicalic oxygen atoms on pseudoeriocitrin are responsible for a number of hydrogen bonds, it should be researched whether normal double-bonded oxygen atoms, in spite of radicalic oxygen atoms, could create the same inhibition effect.” Make a separate heading titled “Future Directions and Limitations” and elaborate on this statement in this paragraph.
8. In the introduction, mention if any laboratory or other research groups have tried to isolate/synthesize this molecule, why or why not?

9. Any known toxicity associated with eriocitrin and pseudoeriocitrin needs to be addressed in the paper. The absence of hydrogen donors raises toxicity concerns that need to be addressed.
10. Performing docking studies and presumably saying a molecule is a great therapeutic is insufficient. Bioassays need to be mandatorily performed as predictions using docking need validation.
11. Having pseudoeriocitrin compared to a standard anthelmintic is also important. Does this molecule have more/less interactions than the standard? What are the bonds that are absolutely needed between the drug and ligand to show anthelmintic effect? What bonds improve efficacy/decrease efficacy? An SAR study and comparison with a marketed anthelmintic is needed.

Overall, I like the insight and approach of the paper. However, I am not thoroughly convinced as a reader about pseudoeriocitrin's role as a therapeutic agent due to lack of sufficient evidence/data. If the authors can address these concerns, this paper has the potential to be cited several times, owing to its innovative approach, which will therefore also increase the visibility of the journal as a whole.

Best,

Giselle Borges e Soares.