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.

Review of the manuscript having the title “Inhibition Success of a Virtually Created Molecule: Pseudoeriocitrin and Femtomolar Inhibition”

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submitted to Qeios for publication.

The authors of the present manuscript report an interesting study using a virtual molecule, “Pseudoeriocitrin,” that they designed and considered through an *in silico* approach, keeping the performance of Eriocitrin in mind. Certain portions of Eriocitrin, a molecule that exists in reality, were modified to see if “Pseudoeriocitrin,” generated *in silico*, performed better by interacting with proteins or whatever biological target authors chose to work with. “Pseudoeriocitrin,” during such *in silico* docking studies, turned out to be better in performance than eriocitrin with regard to different forms of biological, or more specifically, biophysical modes of inhibition. The study aimed to find out what could be the reason for the superior inhibitory activity of “Pseudoeriocitrin,” which was realized at the femtomolar scale. 3D analysis suggests that different interactions were tried through *in silico* protein-ligand docking methods that also seem very interesting. As correctly pointed out by various aspects of the intended study, that, although it is extremely difficult to say anything definite, certain predictions made with regard to “Pseudoeriocitrin” could lead to an interest in synthesizing such molecules or employing such approaches in other areas of drug development where, by using *in silico* approximations, one could synthesize a molecule having specific biological functions; in this case, a molecule with an ability to target nematodes or helminthic infections. The pros and cons of taking “Pseudoeriocitrin” forward could then be worked out based on experimental (i. e., practical laboratory results obtained with Eriocitrin). The new molecule that can inhibit various proteins at the femtomolar level was predicted to be responsible for high binding ability due to its planar structure and its ability to generate lots of oxygen radicals that provide a number of hydrogen bonds with atoms at the active site of proteins.

However, in their approach to *in silico* investigations, why was the structure of “Pseudoeriocritin” not shared as a part of the manuscript, although its description and the points of its difference with Eriocritin were mentioned?

Besides, before moving ahead with docking studies, why is the step showing energy minimization of “Pseudoeriocitrin” not provided or performed? Since there can be multiple conformations for “Pseudoeriocitrin,” it would be extremely essential to know the conformation in which the molecule is most likely to take part in the docking studies that were performed.

Otherwise, what could be realized from the study is that the molecule's large core structure, abundance of oxygen atoms, planar coordinates, and femtomolar level of inhibition were related to each other. The study should definitely lead to a possibility of synthesis of "Pseudoeriocitrin." Effort should be made to find out if this molecule has a chance of being formed during metabolism or could be synthesized in the laboratory, since the formation of "Pseudoeriocitrin" in the body, even for a short time, would inhibit different enzymes without involving any covalent bonding, even at very low concentrations. Some of the information shared in this study is new and useful to design new potent inhibitors. These could be exploited to obtain an inhibitor that would have the ability to inhibit different enzymes at the femtomolar level.

Although there is clarity in communication, yet there are places where the use of the English language was slightly problematic. These things should be seriously looked into before the manuscript can be recommended for publication.