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

Holger Stark[1]

1 Heinrich-Heine Universität Düsseldorf

Potential competing interests: No potential competing interests to declare.

Qeios

Inhibition Success of a Virtually Created Molecule: Pseudoeriocitrin and Femtomolar Inhibition

Dilara Karaman[1], Ahmet Onur Girişgin[2], Oya Girişgin[2]

The authors deal with in silico calculation of a in silico designed molecule on proteins of nematode infection.

The calculated interactions of the natural compound eriocitrin and pseudoeriocitrin were on 10 proteins calculated in 15 calculations in a nanomolar concentration range or below.

The structures and interactions of the proteins are not shown in detail, which is needed at least in Suppl. Mat. Some structures were not reported and have been constructed. In times of AlphaFold-2, the differences between the self-calculated and the AlphaFold structures should be discussed to demonstrate advantages.

Eriocitrin is commercially available. Therefore, some easy experiments can be performed on nematodes, etc., to demonstrate inhibitory interactions.

The structure of the claimed pseudoeriocitrin is not clear. The description in the text claims an isomeric compound, whereas its structure in Fig. 13 shows a totally different compound.

Numerous points lead to a direct rejection of this manuscript for this reviewer:

The structure and structural differences of both compounds investigated are not clear. In the modelling, the authors showed an sp2 planar orientation for the rutenoside-based sugar with sp3 fragments. This takes place with all figures and calculations and is clearly wrong.

The interaction of a small molecule and a protein must be shown in detail. This is very difficult to follow in the actual manuscript. If the interaction potential is calculated, these data are transformed into Ki values without any references.

Eriocitrin has been tested in in vivo studies without any detection of this interaction as a dietary supplement . This gives another reasonable doubt about the claimed interactions – even if eriocitrin is several log units higher in affinity.

Affinity does not automatically reflect inhibition. It can also be activation, etc.

The compound claimed should have very low solubility, whereas the rutenoside flavanone is highly soluble.

These misinterpretations of modelling based on a non-correct structure can be expanded in many points for this manuscript.