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

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Potential competing interests: R.A. received consultancy or speakers' fees from UCB, Sandoz, Abbvie, Zentiva, Teva, Laropharm, CEGEDIM, Angelini, Biessen Pharma, Hofigal, AstraZeneca, and Stada

The title uses "inhibition" redundantly twice and seems rather confusing: it mentions "femtomolar inhibition," but in our view, "inhibition at femtomolar ranges" would have been clearer.

"It gave femtomolar results during in silico docking studies, being more successful than eriocitrin in inhibition." Probably the authors intended "being more successful than…".

"The frequent recurrence of infections among people living in areas with inadequate sanitation, and especially among preschool-aged children, increases the importance of alternative treatments to replace synthetic drugs." This sentence seems to be a non-sequitur. It is not clear to us why the frequent recurrence of infections increases the importance of "alternative treatments to replace synthetic drugs."

"It was formed by the addition of O-β-rutinoside at the 7th position to eriodictyol." "Rutinoside" is a heteroside; therefore, this sentence is incorrect (the text should mention the addition of rutinose, a disaccharide). It should be phrased as "It is formed by the addition of O-β-rutinose at the 7th position to eriodictyol."

"Homoeriodictyol and homo- eriodictyol-7-O-glucuronide are the major metabolites of homoeriodictyol, hesperetin, and glucuronide metabolites." This sentence seems wrong and is difficult to understand (it is hardly understandable how homoeriodictyol could be a metabolite of "glucuronide metabolites").

hERD-7-*O*-Gluc reached approximately 8 ng/g in blood plasma 10 hours after administration, and hERD-4'-*O*-Gluc reached approximately 2 ng/g after 6 hours, the highest levels in blood." What is hERD in this sentence? Abbreviations should be defined with their first use.

"…in our previous study which yielded in silico outcomes." Probably "in our previous in silico study" would have been clearer.

The aim of this study was to show the structure and interactions of pseudoeriocitrin, to which it owes its very high score values, possibly related to its anthelmintic activity."

"Hence its interactions with anthelmintic target proteins researched in silico are thoroughly new and original." It is research/creations of the human mind that can be original, not interactions.

“anthelmintic drug target rat carnitine o-palmitoyltransferase”. Actually, carnitine o-palmitoyltransferase seems to be a chokepoint in nematodes, but its rat version is not (directly) relevant for nematodes. Although the authors stated previously that they used nematode targets and their human homologues, in this case they apparently only used the rat version of this enzyme. Moreover, in the Results section, the authors claim an inhibition constant of 15.83 femtomolar, although it is not at all clear how they managed to estimate it (as docking is in its typical form not able to estimate inhibition constants). If the estimation was correct (which one has little evidence on which to believe), this would rather generate concerns that the substance is not sufficiently selective and that, in fact, it could have adverse effects. The authors should discuss the potential differences between the rat carnitine o-palmitoyltransferase and the helminth carnitine o-palmitoyltransferase and the potential clinical consequences of inhibiting the human carnitine o-palmitoyltransferase (because it is more likely that if the substance inhibits the rat protein, it will also inhibit the human protein).

The situation is similar for fumarate reductases. The authors claim that both the Ascaris suum and the human enzymes are inhibited by pseudoeriocitrin, but they do not discuss the implications of this apparent lack of selectivity.

“The ring structure formed by the formation of an extra bond…”. The tautology “formed by the formation” should be avoided.

“Interestingly, this molecule was predicted in first looking that can penetrate…” – this phrasing should be improved for clarity and grammatical correctness.

“If Pseudoeriositrin's femtomolar inhibition value…”. The name of the flavonoid should be corrected.

“amazing inhibition ability” is a phrase not very appropriate for scientific writing, where one expects sobriety of style and avoidance of exaggerated language.

The authors have provided no evidence of docking validity. One would have expected to see reported the docking results at least for the ligands available in the crystallographic structures of the proteins used.