

Reviewer 3

Comments and Suggestions for Authors

The manuscript: "Human 14-alpha demethylase (CYP51A1) is a putative target for anti-cancer flavonoids" by Leonid Kaluzhskiy et al., contains valuable results that help the understanding of the potential value of flavonoids as anticancer agents. Nevertheless, it needs major revision before be accepted in Molecules Journal.

1. Reviewer 3 commentary:

Enzyme activity assay must incorporate more than one concentration of the flavonoids tested to have a reliable view of the inhibition activity reported.

Authors response:

We performed the additional experiments on concentration-dependent inhibition CYP51 by luteolin 7,3'-disulfate and estimated IC50. As a positive control we used ketoconazole. The information is included in the Results and Materials and Methods sections. (line № 154, 261, 355)

2. Reviewer 3 commentary:

Furthermore, biochemical assays to determine the kind of inhibition must be presented to help to better understand the results presented in this manuscript.

Authors response:

To study the inhibition type of luteolin 7,3'-disulfate along with others flavonoid derivatives and their possible modulation of CYP51 interaction with redox partner is planned as separate follow up research.

3. Reviewer 3 commentary:

The results and discussion section contains basically the results and just a poor discussion. This sections could be divided in order to offer to the readers a better understand and perspective.

Authors response:

The result and discussion are now separated.

4. Reviewer 3 commentary:

The title could be more specific to the compounds tested and not as broad as "anticancer flavonoids".

An alternative is to include in discussion section other flavonoids with the same structure features as those contained in the molecules tested.

Authors response:

Corrected accordingly. The title "Human 14-alpha demethylase (CYP51A1) is a putative target for anti-cancer flavonoids" was changed to the "Human lanosterol 14-alpha demethylase (CYP51A1) is a putative target for natural flavonoid luteolin 7,3'-disulfate"