

Peer Review File

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Reviewer A

Sometimes Tryptanthrine is confused with Tryptamine, that is a totally different compound. Also sentences are sometimes not conclusive and ending blind, presumably because of correction which has been disturbed. No reference to ethnopharmacology can be seen, since Tryptanthrine is purchased in pure form, recommend to skip that part in abstract, one can use that space better, because that topic of antiangiogenesis is interesting. Also there is a longer history on its apoptosis inducing properties, not only dating to 2015 or so, even in china there were early authors who have done research on that. Literature need to be consulted. Plant species were not correctly issued. What is Persicaria? Which of the exact species? Sometime error is really big. If one cannot procure better data, this has to be addressed in the discussion or so.

Comment 1: Sometimes Tryptanthrine is confused with Tryptamine, that is a totally different compound.

Reply 1: Thanks very much for this important comment. We revised “Tryptamine” to “Tryptanthrine”.

Changes in the text: See Page 13, line 262 and line 263.

Comment 2: Also sentences are sometimes not conclusive and ending blind, presumably because of correction which has been disturbed.

Reply 2: We added some contents to make the description smooth and natural.

Changes in the text: See Page 4, line 59- 60, line 62- 63.

Comment 3: No reference to ethnopharmacology can be seen, since Tryptanthrine is purchased in pure form, recommend to skip that part in abstract, one can use that space better, because that topic of antiangiogenesis is interesting.

Reply 3: Special thanks to you for your good comments. We revised the subtitle “Ethnopharmacological relevance” to “Background”.

Changes in the text: See Page 2, line 30.

Comment 4: Also there is a longer history on its apoptosis inducing properties, not only dating to 2015 or so, even in china there were early authors who have done research on that. Literature need to be consulted.

Reply 4: We added a literature about apoptosis property and an updated literature to support it.

Changes in the text: See Page 4, line 66- 67.

Comment 5: Plant species were not correctly issued. What is Persicaria? Which of the exact species? Sometime error is really big. If one cannot procure better data, this has to be addressed in the discussion or so.

Reply 5: We deleted the description of plant species of tryptanthrine.
Changes in the text: See Page 4, line 62-63.

Reviewer B

1. All abbreviated terms should be explained for the first appearance in the Abstract and the main text. qPCR in the text for example. Please check through and revise.

Reply: We defined the abbreviated “qPCR” for the first appearance in the Abstract and the main text. We also defined the abbreviated VEGF in the main text.

Change in the text: See line 101-103 in the revised paper.

2. Figures and Tables

(1) Please indicate the observation methods and the magnification (the scale bars are not clear enough to distinguish) for **Figures 2A, 3A, 3C, 5C, and 5D**.

Reply: We added the observation methods and the magnification in the Figures legend as advised. Please find the attached figures.

(2) Please indicate the meaning of “**” “***” in **Figure 2’s** legend.

Reply: We defined the “**” “***” in **Figure 2’s** legend

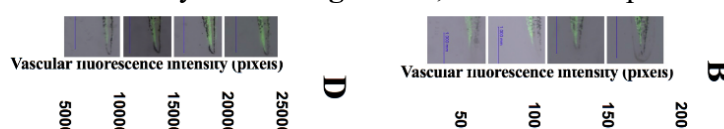
Change in the text: See line 448-449 in the revised paper.

(3) Please indicate the meaning of “**” “***” “****” in **Figure 3’s** legend.

Reply: We defined the “**” “***” “****” in **Figure 3’s** legend.

Change in the text: See line 456-458 in the revised paper.

(4) The words in the y-axis of **Figure 3B, 3D** are incomplete.



Reply: We completed words in the y-axis. Please see attached Figure 3B, 3D.

(5) Your Figure 3E and F legends are the same. Please revise.

456 E: Statistical diagram of intact ISVs in 48-hpf zebrafish ←

457 F: Statistical diagram of intact ISVs in 48-hpf zebrafish ←

Reply: We corrected the Figure 3F legend.

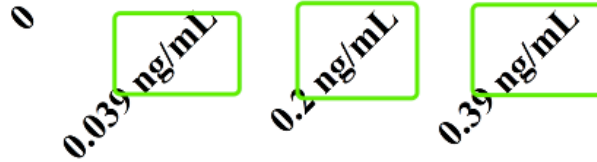
Change in the text: See line 458 in the revised paper.

(6) Please indicate the meaning of “*” “**” in Figure 4’s legend.

Reply: We added the definition of “*” “**” in Figure 4’s legend.

Change in the text: See line 462-463 in the revised paper.

(7) The units are wrong in Figure 4. It should be “ $\mu\text{g/mL}$ ”. Please revise.



Reply: We modified the “ng/mL” to “ $\mu\text{g/mL}$ ”. Please see attached Figure 4.

(8) There is no “*” in Figure 5 while it was explained in its legend. Please check and revise. And please indicate the meaning of “****” in Figure 5’s legend.

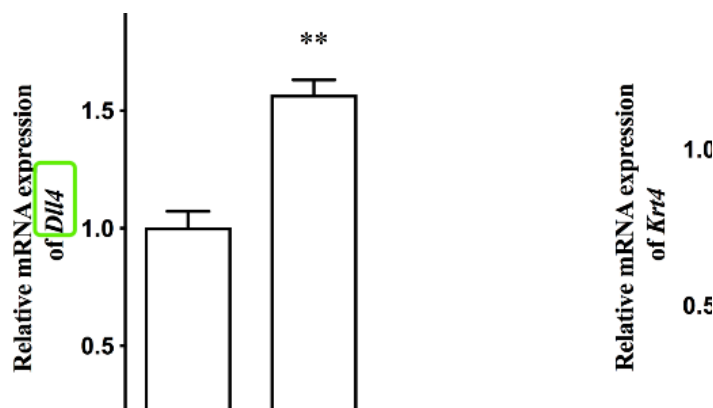
Reply: We deleted “*” definition and added the “****” definition in the revised Figure 5’s legend .

Change in the text: See line 481-482.

(9) Please add a description of the y-axis in Figures 5E, and 5F.

Reply: We checked and added the definition of all y-axis in Figures 5. Please see attached Figure 5.

(10) Figure 7B: There are two same Dll4 expression. One should be “Tnnt2c”. Please revise.



Reply: We modified this error, please see attached Figure 7B.

(11) Please indicate what data is presented in Table 2. E.g., mean \pm SD.

Reply: We added the data presentation in the “Table 2”.

Change in the text: See Page 20, line 437 in the revised paper.