Reviewer’s report

Title: Psychopharmacological effects of riparin III from Aniba riparia (Nees) Mez. (Lauraceae) supported by metabolic approach and multivariate data analysis

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Reviewer: Huiming Gao

Reviewer's report:

The manuscript describes an important tool to prove the anxiolytic-like effect of riparin III in a more efficient and pragmatic way, using 1H NMR urine metabolic footprint combined with multivariate data analysis. Even though the topic is of interest, the present work needs to be further improved. Especially, the following questions are to be carefully considered.

1 The pharmacological activities of riparin III and its similar compounds (riparin I, riparin II, Riparin A) have been presented in the background section. However, there is no significant effect observed based on the present behavioral tests at the tested dosage of 5mg.kg-1. Is the difference induced by various dosage? or other factors? It's better to give the reasonable explanation.

2 The comparative analysis between CP and AP groups presented the establishment of model and the significant difference between AP and TP indicated the effect of riparin III. Is it necessary to compare CP and TP when analyzing and discussing the data of behavioral test or the concentration of the metabolites?

3 The positive drugs treated group is not used. It's important for the evaluation of psychopharmacological effects of riparin III.

4 1H NMR technique has become a rapid metabolic tool now. What's the reason that only five significant components were differentiated, including cortisol, creatinine, riparin III, 5-hydroxy-L-triptophan and allantoin? How many biomarkers or component type were identified from 3 different periods based on 1H NMR data?

5 Fig.5 (d) gave the loadings graphic of urinary metabolites responsible for the differentiation of the 3 analyzed periods (CP, AP and TP). 1H NMR spectrum of urine samples of each period was also necessary to take on the whole metabolite profile of each group.

6. Page 11, line 232, AP-o should be AP-c.
Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
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Yes

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