Reviewer's report

Title: Neuroprotective effect of the hairy root extract of Angelica gigas NAKAI on transient focal cerebral ischemia in rats through the regulation of angiogenesis

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Reviewer: abedin vakili

Reviewer's report:

In this manuscript entitle: "Neuroprotective effect of the hairy root extract of Angelica gigas NAKAI on transient focal cerebral ischemia in rats through the regulation of angiogenesis" authors have reported that root extract of Angelica gigas neuroprotective effect against cerebral ischemia maybe via increase of expression of vascular endothelial growth factors and tight junction proteins and the astrocytes/microglia activation.

However, before publication this paper would need substantial revision (Major revision). Those items needing to be addressed include:

1. Ms has not page number.
2. Abstract part of M.S material and methods is missed. Abstracts should be revised and amended.
3. The introduction of the M.S is somewhat ambiguous and has not fluently and constantly expressed. It is needed to be relevant.
4. What is the reason for choosing hairy root extract of Angelica gigas for studying cerebral ischemia? Please further clarify.
5. In these sentences "All animals were randomly divided into five groups: 1. sham-operation (Sham); tMCAO group with saline treatment (vehicle); MCAO group treated with AG extract at doses of 10, 25, 50, 100 mg/kg (i.p)" Rats was six group not five groups.
6. Timing of AG extract administration to the rats exactly expressed.
7. Number of animals were used in each experiment (infarct volume, brain edema, BBB permeability,...) separately stated. Animal groups were described with more detail.
8. Method of induction of MCAO is not reliable without Laser-Doppler Flowmetry. It is important in absence of monitoring of CBF by Laser-Doppler Flowmetry for MCAO and induction focal cerebral ischemia by filament methods. Animals were randomly assigned to the different treatment groups and the investigator who performed animal surgery was blinded to the treatment of the groups. Apparently, investigators were not blinded to treatment protocols.
9. The authors did not measure cerebral blood flow. Without CBF measurement there is not confidence that ischemia has been attained and interpretation of the
data difficult.

10. It seems method of Statiscall analysis is not corrected. It is need to verify normality test for all of Variable. If normality test is fail, Author should be use from non-parametric test for statically analysis and normality test is pass, Author should be use from parametric test. I have highly recommended consulate with a statiscal specialist. Statistical analysis should be present for each variable separately and again analysis.

11. The authors did not report any mortality. Was there no mortality, or was it not reported.

12. What is the lethal dose of AG extract, and whether AG extract can pass the blood brain barrier?

13. Why AG extract at doses of 10 and 25 has not reduces brain damage and also BBB permeability but reduces cerebral edema.

14. Why in the figure of 4a protein beta-actin is not correct expression.

15. In clinical trials, neuroprotective efficacy is measured by neurological function (Schaaret al., 2010). Why neurologic function has not been investigated in this study.

16. The discussion of Manuscript is repetition of the results and Introduction parts. Discussion part is need to major revision and re-Wright.

17. Professional language editing for grammar and spelling is recommended.

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Not suitable for publication unless extensively edited

**Statistical review:** Yes, and I have assessed the statistics in my report.