Author's response to reviews

Title: Astragalosides from Radix Astragali benefits experimental autoimmune encephalomyelitis in C57BL/6 mice at multiple levels

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Response to reviewer’s comments

Reviewer 1: Fulvio D’Acquisto
Reviewer’s report:
This is a simple and straightforward study assessing the effects of the extract of a plant used in Chinese medicine in a mode of autoimmune chronic inflammation.
The paper is clearly written and the results convincing.
As the authors pointed out themselves, multiple and not necessarily correlated mechanisms might be responsible for the therapeutic effects of the extract.
Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests: I declare that I have no competing interests.
Response:
Thanks for the reviewer’s comments.

Reviewer 2: Altino Choupina
Reviewer’s report:
Discretionary Revisions
The question posed by the authors is well defined.
The methods appropriate are and well described.
The manuscript adheres to the relevant standards for reporting and data deposition.
The discussion and conclusions are well balanced and adequately supported by the data.
Are not limitations of the work clearly stated.
The authors clearly acknowledge any work upon which they are building, both published.
The title and abstract accurately convey what has been found.
The writing is acceptable.
I recommend standardizing the size and type of letters in figures.
In conclusion, the paper explores an interesting topic is well written and I recommend its publication in the prestigious Journal: BMC Complementary and Alternative Medicine.
Level of interest: An article of importance in its field.
Quality of written English: Acceptable.
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests.
Response:
Thanks for the reviewer’s valuable comments. We’ve already tried our best to standardize the size and type of letters in figures of our manuscript in accordance with the requirement of the journal.
Reviewer 3: Zhaoxiang Bian
Reviewer’s report:
This study tested the effect of AST on the progression of experimental autoimmune encephalomyelitis, and its potential mechanism. The study design is acceptable in general. The question is there is no clear research path, and no specific focus. The results showed that multipathways are involved, but what is the linage among them and its relationship with AST is not clear. From this point of view, I am not confident to accept this paper.
Level of interest: An article of insufficient interest to warrant publication in a scientific/medical journal.
Quality of written English: Needs some language corrections before being published.
Statistical review: No, the manuscript does not need to be seen by a statistician.
Declaration of competing interests: I declare that I have no competing interests.
Response:
Thanks for the insightful opinion of the reviewer. First of all, we have to apologize
not to give enough background information of the pathogenesis of MS/EAE in our manuscript. Actually, MS is a complicate autoimmune caused neurodegenerative disease. The general theorem indicates that peripheral immune systems, especially T helper cells such as Th1 and Th17, are abnormally activated when they encounter specific antigens from CNS. Once they are activated, the T cells will induce the breakdown of BBB, thus enter the brain parenchyma where they meet with antigen presenting cells and result in secondary wave of immune response. The reaction leads to further enhanced inflammatory response in CNS such as gliosis. Accordingly, the levels of inflammatory mediators including TNF#, IL1#, IL6 and NO, therefore, ROS will be elevated, which in turn results in the injury of neurons, possibly via induction of their apoptosis. So at the beginning, we did not know at which level astragalosides affected the progression of EAE. To have a general view of the alleviative effect of AST on EAE, we investigated multiple possible targets that might influence the process, which included several pathways in control of T cell differentiation, prevention of BBB breakdown, reduction of ROS, and neuroprotection. To our surprise, AST showed more or less effects in almost all the parameters we examined. Considering the properties of traditional Chinese medicine, i.e. multi-targets and multi-efficacies, and the feature of AST, a mixture of many kinds of saponins, the attenuation of AST on EAE might reflect the comprehensive, perhaps synergistic, effects of individual astragaloside within AST. As pointed out by the reviewer, we admitted that this manuscript merely gave the general efficacy of AST on multiple levels that involved in the progression of EAE without a specific focus even linkage among the effects. But actually, we did those assays in an invisible logic way according to the pathogenesis of MS. The effects were evaluated in a way from peripheral T cell differentiation, to BBB breaking down, neuroinflammation and neuroapoptosis in CNS. Moreover, we’re currently seeking to uncover the deep mechanisms underlying the therapeutic effect. Due to the limitation of the length of the article, we can not provide more detailed information about our recent progress in this regard. If the reviewer is interested, we do invite the reviewer to care about our coming publication about the delicate regulatory mechanism of astragaloside IV, one of the components of AST, on counteracting neuroinflammation with specific binding targets in CNS. Currently, we do ask for the forgiveness from the reviewer about the incompact mechanism of AST on the progression of EAE in this manuscript.

In terms of written English, we’ve tried our best to correct the manuscript and make it look concise and clear for a scientific article.