Reviewer's report

Title: Neuroprotective effects of Eucommia ulmoides Oliv. and its chemical compounds for treatment of Parkinson's disease via ameliorating ubiquitin proteasome system

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Reviewer: Deyan Luo

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Review:

The manuscript by Wang et al demonstrates that Eucommia ulmoides Oliv play the neuroprotective role through ameliorating ubiquitin proteasome system against Parkinson's disease (PD). The results showed that Tanshinone I, one of active compounds of traditional Chinese herb Radix Salviae Miltiorrhizae, selectively suppressed pro-inflammatory M1 genes expression (NO, TNF-#, IL-1# and IL-6) in activated microglia. Meanwhile, it partially reserved anti-inflammatory M2 genes (IL-10, IL-1Ra, CD206) expression. Furthermore, it could provide neuroprotection in a mouse model of Parkinson's disease. From these results, the authors suggest that Tanshinone I could make the most of the beneficial side and minimize the detrimental side of activated microglia simultaneously, and it is a promising strategy for discovering neuroprotective drug targeting microglial activation.

The study is well conducted and based on experiments with PD mice in vivo and SH-SY5Y cell lines in vitro. Male C57BL/6 mice were intraperitoneally injected MPTP with five consecutive injections to induce PD model in vivo. The mice were performed the pole and traction tests to evaluate motor deficits and bradykinesia after final MPTP administration. The PD mice were used to test the compound. To further explore the bioactive constituents and protective mechanism of Duzhong, seven compounds from Duzhong were studied on SH-SY5Y cell lines in vitro.

Comments

This is an interesting paper providing new evidence that Tanshinone I can provide neuroprotection by modulating the immune response of microglia. The present experiments are well designed and the suitable discussion also be done supported by the data presented. However, the reviewer has several specific comments.

Specific comment 1. There are some minor mistakes need to be addressed.

For example: A, the usage of “control” and “vehicle” should be consistent in the whole manuscript;

B, some methods, such as liver toxicity, should be described more detail;
C, there are some of spelling mistakes, and please also revise your English writing.

D, All abbreviations must be spelled out in full at their initial appearance. The reviewer advises that the authors should go over the manuscript carefully before publication.

Specific comment 2. It would be important to give a brief summary in discussion section for Tanshinone I on clinically translational or therapeutically developmental perspectives, molecular structure, chemical features, especially, penetration through blood-brain-barrier.

Specific comment 3. In Fig 4a, the nuclear translocation of p65 by immunocytochemistry is not clear. The authors should provide higher resolution figures. The blurred Fig 5c is not very convincing. The authors should provide a larger, high quality picture for the readers to see in detail. Moreover, the graphical abstract should also be polished.