Author's response to reviews

Title: Neuroprotective effects of Eucommia ulmoides Oliv. and its Bioactive Constituent Might Work via Ameliorating Ubiquitin Proteasome System

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Author's response to reviews: see over
Cover letter

**Title:** Neuroprotective effects of *Eucommiae Ulmoides* Oliv. and its chemical compounds for treatment of Parkinson’s disease via ameliorating ubiquitin proteasome system

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**Key words:** *Eucommia ulmoides*; Parkinson's disease; ubiquitin proteasome system

**Declaration:**
This manuscript/data has not been submitted elsewhere for publication.
All of the listed authors have read and approved the submitted manuscript.
The present study was performed according to international, national and institutional rules.
Dear editor,

This is a revision of the manuscript submitted in BMC Complementary and Alternative Medicine entitled “Neuroprotective effects of Eucommiae Ulmoides Oliv. and its chemical compounds for treatment of Parkinson’s disease via ameliorating ubiquitin proteasome system” (ID: 1235502227142721). Thank you for your letter and for the comments of reviewer 2. We have studied the comments carefully and have made correction that we hope meet with approval. The changes were marked-up by the function of amendment in the revision. The remainder of this letter contains the full text of the editor’s comments (in bold), followed by our responses.

To reviewer 2:

• Major Compulsory Revisions:

1. “Statement made on lines 248-250: I do not believe this statement is backed by the experiments/data presented. It should either be removed or adjusted to fit the data - this compound does NOT show it is important for developmental process in the motor system but it does show that it can prevent damage that leads to motor deficits.”

We completely agree with the reviewer’s recommendation and thank the useful suggestion. This statement is not backed by the experiments/data presented. So we removed it in the revision.

• Minor Essential Revisions:

1. “Still needs help with English language correction - happy to email my corrections directly to the authors or editors.”

We apologize for our poor English writing in the manuscript and sincerely thank the reviewer’s corrections.

2. “There is no reference to Figure 1 in the manuscript until the middle of the discussion- it should be included either in the Materials section (to define "compounds" - mentioned without clarification on lines 185 & 196) or the
author's need to add a small section in the Results to include this important information before showing results related to them or possibly include a small description in the Introduction about where the compounds originate.”

We thank the reviewer for the comment and apologize for our unclear describe the compounds originate until the middle of the discussion in our original manuscript. We have clear described the compounds on the Materials section in the revision. As follow: Professor Su’s group (Tianjin University, Tianjin) isolated eighteen compounds from ethanol extracts of Eucommia ulmoides and identified structures of sixteen. A detailed isolation procedure of these compounds referenced in the paper of Yin [12]. We selected seven compounds (Table 1) with molecular weight under 500g/mol in vitro. They are betulinic acid (Bea), Betulin (Bet), wogonin (Wog), oroxylin A (Oro), genipin (Gen), geniposidic (Ged) and aucubin (Auc). The chemistry structures were shown in Fig. 1 and the purities 98% were verified using High Performance Liquid Chromatography-Ultraviolet Detector (HPLC-UV) analysis. All tested dosage of these compounds was at 10µM. They were dissolved in dimethyl sulfoxide (DMSO) at 10mM as stock solution and diluted in culture medium.

3. “The author's did not discuss the use of a range of Du Zhong concentrations in the Materials/methods section. Because this information is shown in Figures 2 & 3 a short description should be included. They only talk about 0.6 g/kg throughout the manuscript.”

We thank the reviewer for the professional comments and suggestion. We have discussed the use of a range of Du Zhong concentrations on the Results and section Discussion section in the revision. We have marked the changes in the revision.

Again, we sincerely appreciate the time and effort by the Editor and Reviewer in the critique of this manuscript.

With best regards,

Hong Guo