

Peer Review File

Article Information: <http://dx.doi.org/10.21037/apm-20-357>

Review Comments

Comment 1: The quality of English is poor, extensive English editing is necessary.

Reply 1: Thank you for your suggestion, which is important to improve our contribution. Based on your suggestions, we have retouched the manuscript and marked with red lines. We have acknowledged the use of medical writing service.

Changes in the text: Please see Page 17, Line 316 “We wish to thank the timely help of Editage Insights Ltd. with language touchups.”

Comment 2: Authors should write the full name of *L. japonica* in the title. In addition in the text of the manuscript for first use, full form should be mentioned.

Reply 2: Thank you for your suggestions. We have corrected this error.

Changes in the text: Please see Page 1, Line 2-4 “Validation of the protective effects of *Lonicera japonica* polysaccharide on lipopolysaccharide-induced learning and memory impairments via regulation of autophagy based on network pharmacology”.

Comment 3: The introduction section should cite some recent studies like, PMID: 29441009; PMID: 30362531; PMID: 32411333; PMID: 32380758

Reply 3: Thank you for your suggestion, which is important to improve our contribution. We have already cited some of the latest research related to this article in the introduction.

Changes in the text: Please see Page 4, Line 51-53 “Currently, effective clinical drugs for the treatment of AD are lacking (4). In the past decade, several therapeutic agents have been assessed by clinical trials, but none of them have cleared these trials (5,6).”;

Line 59-61 “Several regulators are implicated in the main stages of autophagy, such as ATG5, Beclin 1, and class III phosphoinositide 3-kinase Vps34 (9-12).”

and references 4, 6, 12.

4. Kabir, M. T., M. S. Uddin, A. A. Mamun, P. Jeandet, L. Aleya, R. A. Mansouri, G. M. Ashraf, B. Mathew, M. N. Bin-Jumah and M. M. Abdel-Daim. Combination Drug Therapy for the Management of Alzheimer's Disease. Int J Mol Sci 2020; 21(9):3272

6. Uddin, M. S., M. T. Kabir, P. Jeandet, B. Mathew, G. M. Ashraf, A. Perveen, M. N. Bin-Jumah, S. A. Mousa and M. M. Abdel-Daim. Novel Anti-Alzheimer's Therapeutic Molecules Targeting Amyloid Precursor Protein Processing. Oxid Med Cell Longev 2020, 7039138.

12. Uddin, M. S., A. Stachowiak, A. A. Mamun, N. T. Tzvetkov, S. Takeda, A. G. Atanasov, L. B. Bergantin, M. M. Abdel-Daim and A. M. Stankiewicz. "Autophagy and Alzheimer's Disease: From Molecular Mechanisms to Therapeutic Implications." Front Aging Neurosci 2018; 10:1-18."

Comment 4: Write more details about Construction of a protein–protein interaction network.

Reply 4: Thank you for your suggestion, we have already added more details about Construction of a protein – protein interaction network.

Changes in the text: Please see Page 6, Line 98-104 “ Enter the intersection gene in the "Multiple proteins" search box of the STRING (<https://string-db.org>) online database, djust the minimum interaction score of the resulting pattern to 0.400, and hide it from the main network. Connect the nodes to show the core target genes. Use barplot to count the number of nodes connected to each node in the network and export its tsv file, import the tsv file into Cytoscape 3.6.1 software to build a "drug-target-disease" network, set various types of nodes to different colors and shapes, and adjust The font size makes it suitable for observation.”

Comment 5-Authors should take permission to use Figure from KEGG pathway.

Reply 5: Thank you for your suggestion, in order to to better present the enriched results in KEGG, we have redrawn the picture.

Changes in the text: Please see Fig. 3.

Comment 6: Why 95% ethanol was used for extraction?

Reply 6: Thank you for your question. The extraction method of LJP is derived from the article

published before and has been cited in the article.

Changes in the text: Please see Page 7, Line 111 “The LJP was prepared according to a previously published method (26, 27).”.

Comment 7: What is KM mice, its meaning is not given?

Reply 7: Thank you for your suggestion, we have corrected this error. KM mice is the abbreviation of Kunming mice.

Changes in the text: Please see Page 7, Line 119 “ Male Kunming mice (6–8 weeks old) were obtained from the Experimental Animal Centre of Army Medical University (Chongqing, China) and used as the experimental model.”.

Comment 8: What is the basis for the 30, 100 mg/kg doses?

Reply 8: Thank you for your suggestion, the dosage of LJP is calculated according to the calculation. The daily dosage of *L. japonica* is about 5g (brewing), the converted dosage is 0.083g/kg (calculated by the human weight of 60kg). According to the yield of LJP 5.1% (W/W), the daily consumption of LJP is 4.16mg/kg. According to the formula of interspecies body surface area conversion, the equivalent dose of mice is about 37.91mg/kg, so the dose is set to 30, 100mg/kg (3-fold relationship). The same dosage has also been used in the study of honeysuckle polysaccharide intervention in depression in mice

Changes in the text: Please see Page 8, Line 133-138 “The dosage of LJP is calculated according to the calculation. The daily dosage of *L. japonica* is about 5g (brewing), the converted dosage is 0.083g/kg (calculated by the human weight of 60kg). According to the yield of LJP 5.1% (W/W), the daily consumption of LJP is 4.16mg/kg. According to the formula of interspecies body surface area conversion, the equivalent dose of mice is about 37.91mg/kg, so the dose is set to 30, 100mg/kg (3-fold relationship).”

Comment 9: Authors should cite appropriate references in behavioral testing.

Reply 9: Thank you for your suggestion, which is important to improve our contribution. We have already cited some of the latest research related to this article in the introduction.

Changes in the text: Changes in the text: Please see Page 9, Line 153 “ Alternation performance

above chance level (50%) was indicative of functional spatial working memory [\(28\)](#).” and Page 10,
Line 174 “...was used to track system records and analyze activity [\(29\)](#).”

Comment 10: Data for Western blotting should be provided.

Reply 10: Thank you for your suggestion, which is important to improve our contribution. We have provided the WB data in the attachment.