Author’s response to reviews

Title: Mechanism of Piper laetispicum extract (EAE-P) during Chronic Unpredictable Mild Stress is mediated by the interrelationship of inflammatory cytokines, apoptosis cytokines and neurotrophin in the hippocampus

Authors:

Hui Xie (xiehui@fudan.edu.cn)
Di Jin (kagome1987@163.com)
Yun Kang (ykang@fudan.edu.cn)
Xueru Shi (shixueru@fudan.edu.cn)
Hongrui Liu (liuhr@fudan.edu.cn)
Haixing Shen (shenhaixing163@126.com)
Jian Chen (jianchen_49@yahoo.com.cn)
Macheng Yan (ymc540312@126.com)
Juan Liu (liujuan1949@163.com)
Shengli Pan (slpan@shmu.edu.cn)

Version: 2 Date: 2 October 2014

Author’s response to reviews: see over
Dear Mr./Mrs./Miss,

We would like to submit our report entitled “Mechanism of Piper laetispicum extract (EAE-P) during unpredictable Chronic Mild Stress is mediated by the interrelationship of inflammatory cytokines, apoptosis cytokines and neurotrophin in the hippocampus” for published in “BMC complementary & alternative medicine”.

We trust our paper will be of interest to your readers. The *Piper laetispicum* C.DC. (Piperaceae) is a traditionally used herb in China for invigorating circulation and reducing stasis, detumescence and analgesia, which distributed in the southern part of China and the southeastern part of Asia. Previous studies by our group demonstrated that the ethyl acetate extract (EAE-P) of *P. laetispicum* possesses a significant antidepressant-like effect at doses higher than 60 mg/kg in Kunming (KM) mice, and proved that was not due to an increase in locomotive activity. To research this mechanism, in the present study, the chronic unpredictable mild stress (CUMS) model in Sprague-Dawley rats was used to further elucidate behavioral changes and corresponding changes in inflammatory cytokines (TNF-α, IL-6, IL-10), apoptosis cytokines (P53, Bax, Bcl2, caspase-3) and neurotrophin (BDNF) in the hippocampus of EAE-P treatment animals. The results suggest that EAE-P is beneficial to the behavioral outcome of the CUMS model animals, and decreased amounts of inflammatory cytokine IL-6 contributed to the antidepressant-like activation of EAE-P in every dosage group (15, 30, 60 mg/kg). In the low dosage group, down-regulated apoptosis cytokine P53 is associated with EAE-P effect, but it is inflammatory cytokine TNF-α that is related to the effect of EAE-P in the high dosage group. Meanwhile, the P53-dependent antiapoptotic effect of EAE-P may not be through Bcl-2 and Bax modulation. Furthermore, EAE-P showed up-regulated expression of brain-derived neurotrophic factor (BDNF) mRNA and down-regulated apoptosis cytokine caspase-3 mRNA, which was the same change tendency as with Fluoxetine.
Professor Shengli Pan is the corresponding author, who can be reached at the address:
826 Zhangheng Road Shanghai, 201203 China. Tel: 86-21-51980137 Fax: 86-21-51980137 E-mail: slpan@shmu.edu.cn; slpan45@126.com

We appreciate your consideration of our manuscript. And this article or any one with similar content has not been submitted to any other journal.

Yours sincerely,

Sheng-li Pan