Author's response to reviews

Title: Toona sinensis leaf extract has antinociceptive effect comparable with non-steroidal anti-inflammatory agents in mouse writhing test

Authors:

Yu-feng Su (suyufeng2000@gmail.com)
YU-CHIAO Yang (m755016@kmu.edu.tw)
HSENG-KUANG Hsu (m585004@yahoo.com.tw)
Shiuh-Lin Hwang (nsdoctor@yam.com)
Kung Shing Lee (leekungshing@yahoo.com.tw)
Ann-Shung Lieu (e791125@gmail.com)
Te-fu Chan (tefu.chan@msa.hinet.net)
Chih-Lung Lin (chihlung1@yahoo.com)

Version: 3 Date: 15 December 2014

Author's response to reviews: see over
Dear editors:

We are grateful to submit the revised manuscript entitled "Toona Sinensis Leaf Extract Has Anti-nociceptive Effect Comparable to Non-steroidal anti-inflammatory Agents in Mouse Writhing Test" to BMC Complementary and Alternative Medicine.

Sincerely,

Chih-Lung Lin M.D.

Department of Neurosurgery, Kaohsiung Medical University Hospital

No. 100, Tz-you Road, Kaohsiung 80708, Taiwan

Tel: 886-7-3215049    Fax: 886-7-3215039

E-MAIL: chihlung1@yahoo.com
For Major Comments

1. The mechanism of the TS or TSL1 in the production of antinociception has not been well established. Earlier evidence has shown that the components of TS exert potent anti-inflammatory, analgesic actions and inhibit boil growth in vivo [1, 2]. Several mediators are responsible for pain and hyperalgesia in inflammation including cytokines, chemokines, nerve growth factor as well as bradykinin, prostaglandins and ATP [3]. In 2013, TS was demonstrated to inhibit viral attachment (Influenza A, H1N1) through significant downregulation of adhesion molecules and chemokines (VCAM-1, ICAM-1, E-selectin, IL-8, and fractalkine) [4]. That’s why we performed this study, trying to show the potential antinociception effect of Toona sinensis. Further molecular study design and analysis are needed to clarify the definite mechanism.

2. Thank you for the correction and reminding. We put in the wrong number about the dosage of Toona sinensis (TS) extract powder in the manuscript (But the dose shown in the Table is correct). Different extraction fractions of leaf extracts from TS (i.e. TSL1 to TSL5) were administered orally 1 hour before acetic acid intraperitoneal injection in dose of 1 g/kg, not 1mg/kg. The re-designed Table 1 showed the result. The control group was fed with “Vehicle” (i.e. double distilled
water) in the dose of 10ml/kg.

3. The most significant antinociceptive effect of TSL1 occurred at dose of 0.1 g/kg. When dose of TSL1 increased more than 0.1g/kg, the antinociceptive effect did not increase in a dose-dependent pattern (Table 1). This data implied possible receptor/ligand-gated mechanisms may involve the antinociceptive effect of TSL1. (The paragraph was added to the Discussion section, page 10, Line 165)

4. Thank you for the comment. Rofecoxib and Diclofenac, are both well studied NSAID, especially about their efficacy, potency as well as safety. TSL1 to 5, extracted from Toona sinensis leaf, is not a pure compound and does not show a definite dose-dependent effect in this study (Table 1). Further study for the efficacy and potency is needed.

5. We did not observe significant side effects or behavioral changes in the present study. However objective and structured evaluation of behavior and locomotor function should be included in the further study. Thank you for the comments.

6. Thank you for the suggestion about the model using 2,4,6-trinitrobenzenesulfonic acid (TNBS). We are also considering the TNBS model in the future study, with the consideration of specificity and animal ethical issues.

1 For Minor Comments
1. Thank you for your comments. This re-submitted manuscript has been edited and corrected by a skillful native English editor. (suggested by the BioMed Central Editorial)

2. The consideration about the potential side effects is important. In this study, we did not observe any changes on behavior or locomotor functions, from TSL1 to TSL5 (with 1g/kg) and the dose from 0.01g/Kg to 0.3g/Kg of TSL1. The observation is added to the Discussion Section, page 11-12, line 184-188. Thank you.

References


To Referee, Bhomik Goel

Thank you for your comment.

The dosage of the plant extract is according to the previous studies. The references are listed below:

