Author's response to reviews

Title: An-jun-ning, a traditional herbal formula, attenuates spontaneous withdrawal symptoms via modulation of the dopamine system in morphine-dependent rats

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

Thank you for your advice for our manuscript titled “An-jun-ning, a traditional herbal formula, attenuates spontaneous withdrawal symptoms via modulation of the dopamine system in morphine-dependent rats”. We have made some changes to the manuscript according to editorial requirements. And the point-by-point descriptions of the changes are as follows.

**Requirement 1**

- We note that Taier company provided the An-jun-ning formula that was used in your study. Could we ask you to confirm whether Taier played any other role in the financing, design, implementation or analysis of your study? If so, please include this information in your Competing Interest section. If not then, in the interests of openness, we would still ask you to include a statement declaring this in your Competing Interests section.

  Taier company did not play a role in this study and have nothing with financing, design, implementation or analysis of this study. So, there are no competing interests with Taier company. We have added the expression of our thanks to Taier company in the acknowledgements section.

Revised in the manuscript:

**Acknowledgements section:**

We thank Taier company for providing AJN used in this study.

**Requirement 2**

- At present, we do not feel that there is sufficient evidence presented in your Background section to justify the testing of An-jun-ning in an animal model of opioid dependence. We would therefore ask you to expand this section to include as much referenced evidence to explain why you would expect this treatment to have an effect
in this model. This evidence should come from previous in vitro or animal work. Please note that we are unable to accept traditional medical use as sufficient justification for animal studies.

We have expanded the Background section (mainly the 2nd paragraph of this section) related to the animal studies evaluating the effect of An-jun-ning in opioid dependence.

Revised in the Background section of manuscript:

Besides, AJN has been proved to possess highly suffertibility and safety (Jing, 2000). Previous studies have find that AJN could upregulate the expression of pre-pro-opiomelanocortin and pre-proenkephalin decreased by morphine in dependent rats (Hongxian SH, 2005&2006). And also, AJN was reported to be able to attenuate the disturbance of tyrosine hydroxylase (TH) and gial fibrillary acidic protein in ventral tegmental area, which implied the key role of dopamine (DA) system in the therapeutic effect of AJN on protracted withdrawal symptoms (Hongxian SH, 2006). Yet the mechanism by which AJN alleviated the DA system has not been studied systematically or completely. So this study was to figure out the involvement of DA system in the effect of AJN in a rats model of morphine dependence.

We thank you in advance for your consideration and look forward to hearing from you.

Sincerely yours,

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