Author's response to reviews

Title: Effect of green tea extracts on oxaliplatin-induced peripheral neuropathy in rats

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Author's response to reviews: see over
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Dr. Rajesh Agarwa
Section Editor, *BMC Complementary and Alternative Medicine*

Dear Dr. Rajesh Agarwa

I am very deeply appreciated about the sophisticated review comments of two reviewers. We corrected the mistakes in the submitted article.

Based on the reviewer's comments, we reanalyzed our data using the percentage of maximal possible effect (%MPE), instead of the latency of tail-flick reactions, and we found the significant differences in thermal response between two groups at 6 weeks after oxaliplatin administration.

Therefore, our study is meaningful to show palliative effect on neuropathic pain induced by oxaliplatin.
To Elizabeth K Joseph

Thank you so much for your helpful comments in our study.

1. *Is the question posed by the authors well defined?*

   : Scientifically speaking, this study does not have great acceptance as use of alternative medicine (therapy) is not well recognized. I have promoted it because I believe in the usefulness or adjunct utility of alternate medicine and there is always room for improvement. But the authors are not strong or specific in their articulation of the purpose of the study. Proclaiming that they were studying the curative effect of Green tea extract against Oxaliplatin induced neuropathy is difficult to accept.

   **Reply** To date, there are no effective therapy to prevent neuropathic pain induced by chemotherapy. The purpose of our study is to find out the palliative, not curative, effect of green tea extract on neurotoxicity symptoms induced by oxaliplatin. We also believe in the usefulness or adjunct utility of alternate medicine. However, there is always limitation of all therapies, when applying the patients who have been regularly taking chemotherapy, suffering from cancer. So, we need to find out the information about the advantage or disadvantage of adjunct utility, which have even somewhat disappointing results.

2. *Are the methods appropriate and well described?*

   : The experimental approach of thermal hyperalgesia is not appropriate. One has to leave enough room (difference in duration between the control and test) in order to evaluate the significance. The authors mention that they have set the intensity to 50% at the beginning and
the latency in the control is low. In that case they would have reduced the intensity to even lower level to understand whether there is significant difference between the control and the oxaliplatin treated group.

**Reply** In review of journals, the thermal stimulation intensity setting was different. If the stimulus intensity were set below 50% and a maximum cut off latency were longer, there would be a high chance of spontaneous tail-flick reactions. The longer maximum cut off latency may severely affects the results of nerve conduction study such as causing delayed latency and decreasing amplitude.

In Encyclopedia of Psychopharmacology (Volume 2, by Ian P. Stolerman), the individual variation of thermal response was noted, which was agreed by authors. So we used the percentage of maximal possible effect (%MPE), instead of the latency of tail-flick reactions, and re-analyzed the data, which showed the significant differences in thermal response between two groups at 6 weeks after oxaliplatin administration.

Thus, our study showed meaningful effect on palliation of oxaliplatin-induced neuropathic pain.

On page 7 & 9 and Figure 3, we corrected the article according to the results.

9. *Is the writing acceptable? Discretionary Revisions:* 
The authors mention in the material and method section that the weight of the animal used for the study as 290-300 g where as in the result section the weight of the animals in the two different groups were: 338 and 352 g. As a whole, there is lack of experience in presenting the data and results, which can be corrected by paying proper attention to the manuscript.
Reply) We performed on 301±7 g adult male rats. Before oxaliplatin administration, the weight of Group I was 303±5 g and that of Group II was 299±8 g. The weights of the rats in Group I increased from 303±5 g to 338±15 g, and the weights of the rats in Group II increased from 299±8 g to 352±20 g during the course of the experiment.

On page 23, we changed the figure legend 1.

Yours sincerely,

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