Author's response to reviews

Title: Effects of JSOG-6 on protection against bone loss in ovariectomized mice through regulation of osteoblast differentiation and osteoclast formation

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Author's response to reviews: see over
Dear Dr. Editor of BMC Complement Altern Med

Thank you for your letter of 3 April 2014, and the comments of manuscript 1059507997115854. According to reviewer’s comments, the manuscript was properly revised as followings.

Reviewer: Anne Blais

Reviewer's report:
In my first report I indicate that the authors do not present any significant difference between the 3 different concentrations of JSOG-6 used. It was my major comment and the authors did not do any modification.

Major Revisions

1. I do not agree with the interpretation of the results. Statistically the authors never showed a dose-dependent effect of JSOG. A dose-dependent may be observed but only for the Tb.No parameter however the authors do not showed any statistical difference between the different JSOG concentrations.

Response: As commented, we looked over the original data carefully and recalculated the parameters. Although Tb.Sp and SMI parameters in the OVX-induced models were increased and the treatments of test materials inhibited the parameters, however, the dose-dependency was not significant. Therefore, the sentences related to the findings in Fig. 1 were newly rewritten on Page 12 and re-depicted in Fig. 1.

The Tb.No in the OVX group was 63.8% lower than that of the Sham group, but JSOG-6 treatment (50, 150, and 450 mg/kg) significantly recovered the Tb.No value to 113.3, 145.6, and 192.2%, respectively, in a dose-dependent manner than the OVX group. The E2-treated group also showed a 150% recovery of Tb.No compared to the OVX group.

2. They report that BMD of trabecular bone of the femur was shown to be 97.4% higher than the OVX. How this value was calculated? I do have the same question for the E2 group (79.5% increase). The figure do not shows any difference between the E2 group and the JSOG treated groups.
Response: The values were calculated as follows:

The data in Fig.1 were BMD (Sham, 0.0633; OVX, 0.0388; E2, 0.0702; JSOG-6, 50 mg/kg, 0.0710). Therefore, the % was re-calculated as followings and indicated on Page 12 line 5 -9.

1) \[1-(OVX/Sham)\] \times 100 = 38.7%
2) \[(JSOG-6/OVX) - 1\] \times 10 = 83.0%
3) \[(E2/OVX) - 1\] \times 100 = 80.9%

3. The authors report a BV/TV reduction by the OVX procedure of 0.71%. The figure shows a reduction of 71%.

Response: As suggested, the value was re-calculated for the data and newly indicated the value as followings. The value was newly indicated on Page 12 line 10.

\[\text{BV/TV (Sham, } 2.01; \text{ OVX, } 0.71)\]

\[1-(OVX/Sham)] \times 100 = 64.7\%

4. Is the Th.Tb parameter is modulated by the OVX procedure? Figure 1 do not shows any difference.

Response: As mentioned in response 1, the value for Th.Tb in Figure 1 was deleted.

5. In Table 2 there is a column for the mean and another one for the SD. A value should be associated to its SD in the same column ex: 91.2 + 0.5. Moreover when the mean is of 91.2 the SD should be of 0.5 not 0.52.

Response: As suggested, the sentence was properly changed in Table 2.
Reviewer: Yin Xiao
Reviewer’s report:

the authors have addressed most issues thoroughly.

Reviewer: Jean Langlois
Reviewer’s report:

Minor Revisions
1. I would suggest authors to add further details in the results part of the abstract.

Response: As suggested, the abstract was newly sentenced as followings.

Oral administration of JSOG-6 significantly increased the bone mineral density (BMD) of the femur in OVX mice in vivo. Especially, the reduced Tb.No (trabecular bone number) in the OVX group was significantly recovered by JSOG-6 treatment. The serum levels of alkaline phosphatase (ALP), osteocalcin, C-terminal telopeptide, and tartrate-resistant acid phosphatase, biomarkers of bone resorption, were significantly elevated in OVX mice, but JSOG-6 effectively inhibited the increase in OVX mice. JSOG-6 was also found to enhance the osteoblastic differentiation and maturation with the increase of the density and ALP activity, a marker of osteoblastic differentiation, as well as calcium deposition, a marker of osteoblastic maturation in MC3T3-E1 cells. The effects of JSOG-6 on osteoblastic differentiation were also associated in part with the increase of ALP and OPN mRNA expressions and the decrease of RANKL mRNA expression in MC3T3-E1 cells.

2. I would suggest that authors would be less confident in the conclusion part of their manuscript. Clinical utilization of the molecule might need to be further tested before being such confident.

Response: The present findings suggest a potential therapeutic strategy of JSOG-6 in the protection of osteoporotic bone loss in clinic. This was indicated in the sentence of conclusions part.

As a result of these changes, the manuscript might be substantially improved and hopefully acceptable for BMC Complementary & Alternative Medicine.

With many thanks for your help and consideration.

With my best regards,

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