Author's response to reviews

Title: Anti-inflammatory and Anti-cancer Activity of Mulberry (Morus alba L.) root bark

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

Please consider for publication in your esteemed journal our manuscript “Anti-inflammatory and Anti-cancer Activity of Mulberry (Morus alba L.) root bark”.

None of the material presented here has been published or under consideration elsewhere.

Main Point:

[RESPONSE for REVIEWER’s Comments]

1. The authors should identify the major active components that exert anticancer and anti-inflammatory effects in MRBE.
   
   **Answer:** Mulberry root bark has been reported to have various active components such as mulberroside A, oxyresveratrol, mulberrofuran G, kuwanon C, kuwanon G, kuwanon H and morusin. Cheon et al (2000) and Yang et al (2011) have reported that kuwanon C and kuwanon G possess an anti-inflammatory effect. In anti-cancer activity, Lee et al (2008) has reported that morusin induce apoptosis and suppress NF-kB in human colorectal cancer cells. It was added in Discussion.

2. How did the authors measure NO level secreted by Raw 264.7? Because there is no data on the cell viability of RAW264.7 treated by MRBE (5-50 ug/ml), how did the authors confirm whether the decrease of cell viability induced by MRBE was due to the inhibitory of NO level or MRBE blocked NO production via suppressing iNOS over-expression in LPS-stimulated RAW264.7 cells?
   
   **Answer:** It has been well known that NO is secreted by iNOS. If MRBE-mediated inhibition of NO production results from the reduction of cell viability, MRBE does not affect iNOS expression. But we found that MRBE attenuates LPS-induced iNOS overexpression in dose-dependent manners and inhibits NO overproduction. Therefore, we could confirm that inhibition of NO overproduction may be consequence of suppression of iNOS overexpression.

3. The authors should explain more clearly about why proteosomal degradation induced by MRBE can promote NF-kB translocation into nucleus.
   
   **Answer:** We have evaluated IkB-a level in RAW264.7 cells treated MREB in absence of LPS treatment. In this experiment, MREB did not affect IkB-a expression (data not shown). However, MREB inhibited IkB-a down-level induced by LPS. So we suggest
that MREB may attenuate LPS-mediated IkB-a degradation.

4. MRBE seems to be a non-polar extracts, what kind of compounds could enter the cells to exert the anti-inflammatory and anti-cancer Activity? The authors should provide more details.

**Answer: See 'Answer' for Q1.**

Thank you for your time and consideration. We look forward to a positive response from you.

Sincerely yours,

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