

## Author's response to reviews

**Title:** Cactus Pear - a Natural Product in Cancer Chemoprevention

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### Author's response to reviews:

Hikomichi Kumagai, M.D.

Deputy-Editor-in-Chief,

Nutrition Journal

Re: MS: 1002452498632539

Dear Dr. Kumagai:

Thank you very much for reviewing our manuscript and the important critiques. We have carefully reviewed the manuscript according to the critiques and revised our manuscript. The revised text is highlighted with bold letter. The following is our answers to the critiques.

1. The experiments for cell growth inhibition, IC50, cell cycle analysis

and apoptosis induction were performed with cactus pear concentration of 0-25%. The results for apoptosis induction were shown only those with 25 %.

Answer: We have put back the figure shows effect of 5% cactus extract on apoptosis, please see revised Fig 3a and 3b. At the concentration of 5% effect of cactus pear on apoptosis was not strong, probably due to its early effect on cell growth arrest. On the other hand, the effect on cell cycle arrest was consistent with that on grow arrest.

Physical properties of cactus pear solution: The osmolarity of the solution was 358 mmol/kg for 25% solution, 342 mmol/kg for 10%, and 326 mmol/kg for 5% (the osmolarity of 10%FBS/DMEM medium was: 312 mmol/kg). The pH was around 7.26 -7.28.

2. The Introduction section should be re-organized and shorten in 1.5 pages.

Answer: We have shortened the introduction.

3. P13, lines 10-12, the reader may feel p53 expression was decreased by

the cactus pear treatment because of 'more negative nuclei were observed'. This part is inconsistent with the description of p15, lines 18-19.

Answer: Expression of p53 was not changed significantly by either 4-HPR or cactus. However, involvement of p53 in cactus-induced apoptosis may not be ruled out by our observations.

4. New references 26 and 27 were added for cell cycle analysis and tumor volume calculation.

5. Figure 1 was revised.

6. Fig 5b. Tumor size unit mm<sup>3</sup> were added in.

7. Statistical analysis were moved at end the methods.

We have checked the manuscript again for spelling mistakes.

I would like to thank you again for your effort and critical review of our manuscript.

Sincerely

Changping Zou, MD, PhD

Associate Professor