

Format for ANSWERING REVIEWERS



October 1, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2wjp-2014-02568488-review-revised.doc).

Title: The potential ability of xanthophylls to prevent obesity-associated cancer

(Previous title: Potential ability of xanthophylls for preventing cancer")

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Name of Journal: *World Journal of Pharmacology*

ESPS Manuscript NO: 12204

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

Yes

2 Revision has been made according to the suggestions of the reviewer. The changed parts are clearly marked in red.

Reviewer No. 00503608

(1) As suggested by the Reviewer, We changed the title of the manuscript to focus exclusively on obesity-associated cancers. Moreover, we added a new Table addressing obesity-associated cancers (Table 1), as appears in the revised manuscript.

(2) The frequent errors of grammar and syntax in the Abstract, Introduction and Conclusions section were corrected using American Journal Experts's editing service.

(3) We added the sentence "As shown in this review, xanthophylls provided health benefits, such as improvements in inflammation, dyslipidemia, hypertension and liver function." in the Introduction section on page 5, lines10-12 of the revised manuscript.

(4) Related to comment (1) of Reviewer No. 00040410, we added Figure 1 illustrating the possible mechanisms for obesity associated cancer prevention. According to this change, Figure 1 in the original manuscript was moved to Figure 2 in the revised manuscript.

(5) As recommended by the Reviewer, we provided some references (ref 8, 9) to justify the statements that that foods or food/plant derived agents may be useful for the prevention and/or treatment of cancers, in the Introduction section of revised manuscript.

Reviewer No. 00040410

(1) Related to comment (3) of Reviewer No. 00503608, we added Figure 1 illustrating the possible mechanisms for obesity associated cancer prevention. This figure aims to simplify the correlation between PPAR, obesity and carcinogenesis and between nrf2 and PPAR. According to this change, Figure 1 in the original manuscript was moved to Figure 2 in the revised manuscript.

(2) As suggested, the words "but we would like to take a light" on page 14, line 10 in the original manuscript were

replaced by “focus”.

(3) Reference No. 93 in the original manuscript is a proceeding of The Japanese Society for Carotenoid Research. Thus, we clearly describe this is a proceeding of The Japanese Society for Carotenoid Research in Reference section of the revised manuscript (Ref No.97).

(4) To avoid misleading the readers, we added the sentence “, nevertheless GGT has no causative role itself.” after the sentence “it has been demonstrated that increased plasma levels of GGT are associated with an increased risk of pancreatic cancer[99,100].” on page 17, lines 12-13 in the original manuscript.

(5) As point out by the Reviewer, we corrected the sentence “Thus, uPA, PAI-1 and uPAR might be used as potential tumor markers for mammary cancer[105], and FX may reduce such a tumor marker.” on page 18, lines 1-2 in the original manuscript, and replaced it by the corrected sentence “Thus, uPA, PAI-1 and uPAR might be used as prognostic markers for mammary cancer[105],” as shown in the revised manuscript.

Reviewer No. 02445225

(1) As suggested by the Reviewer, we searched and overviewed new reports again and improved the reporting of the preclinical and clinical studies as listed below in the revised manuscript.

Astaxanthin: not changed

β-cryptoxanthin: not changed

Fucoxanthin: We added some preclinical reports.

i) Inhibition of PI3K/Akt signals in human cervical cancer cells (ref 92).

ii) Inhibition of NFκB signals in human breast cancer cells (ref 93).

Neoxanthin: not changed

Zeaxanthin / Lutein: We added epidemiological data and some preclinical reports.

i) Reduced risk of oral cavity and pharyngeal cancer (ref 148)

ii) Induction of cell cycle arrest in human prostate (ref 156) and esophageal (ref 157) cancer cell by lutein.

iii) ZX also induced cell cycle arrest in human breast cancer cells (ref 159).

3 References and typesetting were corrected

Yes

Thank you again for publishing our manuscript in the *World Journal of Pharmacology*.

Sincerely yours,

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