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Flat C, 23/F., Lucky Plaza,  
315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 2248

**Title:** Dietary phytoestrogens and insoluble fibers increase estrogen receptor beta expression in the colon mucosa of patients with colonic adenomas. A randomized, double blind, placebo-controlled study.

**Reviewer code:** 00608185

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-02-13 13:23

**Date reviewed:** 2013-02-26 10:20

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

This manuscript is well organized and interesting. I have one question in results. The author described that "In recurrent patients a higher ER-beta protein (p=0.04) and a lower ER-alpha LI (p=0.02), in ADI group, was also disclosed." This phenomenon was seemed to be controversial against the role of ER-beta in this manuscript. Could you explain this matter?



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**Title:** Dietary phytoestrogens and insoluble fibers increase estrogen receptor beta expression in the colon mucosa of patients with colonic adenomas. A randomized, double blind, placebo-controlled study.

**Reviewer code:** 00503495

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-02-13 13:23

**Date reviewed:** 2013-03-08 01:36

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS TO AUTHORS

Mariabeatrice P. et al. reported in the paper entitled, "Dietary phytoestrogens and insoluble fibers increase estrogen receptor beta expression in the colon mucosa of patients with colonic adenomas. A randomized, double-blind, placebo-controlled study," that ER beta protein was upregulated in the colonic biopsies and this receptor was co-localized with caspase-3, leading to the conclusion that ER beta was involved in apoptosis. The idea about using dietary supplements to suppress ER beta-mediated colon tumorigenesis is very interesting. However, these authors failed to provide convincing evidence to support that their dietary supplements make any difference and ER beta plays any role in tumorigenesis. Some specific comments are as follows: 1. Grammatical error on last sentence on p5: "Finally, there is evidence...bind to an activate (?) ER with (?) chemopreventive effects..." 2. Bullet points at the end of introduction (p6) should be revised into sentences. 3. p14: Authors claimed that "none showed high grade dysplasia." What is the significance of slight increase of the ER beta protein then? Authors should elaborate. 4. p15 and Table 2: Authors reported that the increase of the ER beta protein was statistically significant. However, the difference was only marginal with P=0.04, which only very weakly justified that the observed difference is indeed real/interesting. Additional data to support this increase would be necessary. For example, any data to show that this increase in ER beta has functional implication would be good (any increase in target gene expression for example). The fact that ER beta message levels were no difference, suggesting that change of gene transcription and mRNA stability do not explain the increase of the receptor protein and protein degradation might play a role in the difference of the ER beta protein. Authors



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should elaborate about the mechanisms involved in the increase of the ER beta protein with cited literature or data. 5. First sentence under "Treatment-related immunohistochemical biomarkers" - "The median value..." - does not make sense and should not be an one-sentence paragraph. 6. p18: Authors stated that "...correlation tests showed that ER-beta was directly linked to apoptosis." This statement is too strong and authors did not show convincing data to make this conclusion. The co-expression immunohistochemical data per se are not adequate. Some in-vitro (cell culture) data should be helpful to provide useful data. 7. p19 and Table I: Authors stated that "...ADI substantially increased phytoestrogen levels..." which actually weakened the argument that ADI upregulated the ER beta protein. It appeared that ADI was not that effective at all to upregulate the receptor.



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**ESPS Manuscript NO:** 2248

**Title:** Dietary phytoestrogens and insoluble fibers increase estrogen receptor beta expression in the colon mucosa of patients with colonic adenomas. A randomized, double blind, placebo-controlled study.

**Reviewer code:** 00504611

**Science editor:** Gou, Su-Xin

**Date sent for review:** 2013-02-13 13:23

**Date reviewed:** 2013-03-15 00:17

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
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<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

This is an interesting report and while a number of the findings are near-significant rather than being significant, in my view the study should be published and hopefully encourage further, perhaps larger, studies to be undertaken. Although the data is summarised in a reasonable manner, I would have liked to have seen a little more of the initial data to better gauge variation and spread of the values. For the IHC data, was it simply the percentage of cells positive that was evaluated or was there any attempt to look at intensity / strength of staining also? Minor changes to the english are needed in a few places.