

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8818

Title: Inhibitory Effects of Genistein and Resveratrol on Contractile Activity of Isolated Gastrointestinal Smooth Muscle in Rats and the Related Mechanisms

Reviewer code: 00073774

Science editor: Na Ma

Date sent for review: 2014-01-08 21:40

Date reviewed: 2014-03-04 19:24

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 checked="" type="checkbox"/> Grade C (Good)	<input checked="" 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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

The manuscript entitled "Inhibitory Effects of Genistein and Resveratrol on Contractile Activity of Isolated Gastrointestinal Smooth Muscle in Rats and the Related Mechanisms" provides original data revealing the action of genistein and resveratrol on the contractile activity of rat gastric and duodenal muscle strips and the involvement of alpha adrenergic receptors, nitric oxide, potassium channels, cAMP, calcium and estrogen receptors on this action. I have some concerns about the paper which could be summarized as follows: 1) In METHODS section, the experimental protocol needs to be revised. The cumulative administration of resveratrol and genistein in the presence of different agents should be explained in details. The equation of "percentage change" given in the statistical analysis section needs to be clarified (e.g., what is the meaning of "contrast value"?). 2) RESULTS section: Under each subtitle, the numeric data and the significance level of the changes should be given in the text. Additionally, the figures are not easy to follow. Line graphics showing relaxation (%) are recommended for Figures 2,3 and 4 instead of bars. 3) DISCUSSION section is generally poor. The discussion on the findings with estrogen receptor antagonists needs special interest, as the two agents are presented as phytoestrogens. 4) The manuscript needs careful polishing in terms of grammar and spelling.

ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8818

Title: Inhibitory Effects of Genistein and Resveratrol on Contractile Activity of Isolated Gastrointestinal Smooth Muscle in Rats and the Related Mechanisms

Reviewer code: 00573027

Science editor: Na Ma

Date sent for review: 2014-01-08 21:40

Date reviewed: 2014-03-05 23:45

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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This is a nice paper looking at the effects of phytoestrogens genistein and resveratrol on the inhibition of gastrointestinal motility. The data support the conclusions of the authors. Overall the manuscript is well written, however the authors need to polish the English and proof read carefully for grammatical errors.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8818

Title: Inhibitory Effects of Genistein and Resveratrol on Contractile Activity of Isolated Gastrointestinal Smooth Muscle in Rats and the Related Mechanisms

Reviewer code: 00055107

Science editor: Na Ma

Date sent for review: 2014-01-08 21:40

Date reviewed: 2014-03-14 18:34

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 checked="" type="checkbox"/> Grade C (Good)	<input checked="" 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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input checked="" type="checkbox"/> Major revision

COMMENTS TO AUTHORS

This paper describes the inhibitory actions of genistein and resveratrol on gastric and duodenal contractility in rats and studies the pathways involved in these actions, suggesting that alpha1 adrenergic receptors, nitric oxide, K-ATP channels and cAMP are implicated. This is a well conducted work; however, I consider that this paper should be improved at several points shown below. Throughout the text, English grammar should be revised. Methods section: How is measured the contractile responses induced by CaCl₂? Is it the maximal amplitude of the response or the integrated area under the curve? Please specify. The values were analysed using Student's t-test and one-way analysis of variance, but authors did not state in which cases were used each one? Used the authors any test posterior to the one-way ANOVA such as Bonferroni... to compare data from every treatment with that from control value? Discussion section: Discussion is too long, with several paragraphs with information enough known that is not necessary. Some of them can be reduced such as the description of the enteric nervous system, the expression of alpha1-adrenoceptors in tissues outside the gastrointestinal tract and the description of the PLC-DG-IP₃ pathway. In the introduction and discussion sections, authors did not include references to previous papers that showed the inhibitory effects of genistein on the contractile activity of the gastrointestinal tract, that were carried out also in rats and using strips from: - Gastric fundus (Mustafa and Oriowo, 2005, Clin. Exp. Pharm. Physiol. 32:832-838) - Duodenum (Kawabata et al., 2000, Life Sci. 67:2521-2530) - Ileum (Ohta et al., 2000, Eur. J. Pharmacol. 387:211-220) - Colon (Takeuchi et al. 1999. J. Physiol. 514:177-188, Mule et al., 2002, J. Pharmacol Exp. Therap.

303:1265-1272). In all these papers, genistein was used as a known competitive tyrosine kinase inhibitor. Even genistein was added to the bath at similar concentrations than those used in the present paper. Then, I am surprised to the fact that the tyrosine kinase pathway is not referred in the discussion section when other secondary messengers such as cAMP are study in the paper. Authors investigate the pathways involved in the genistein and resveratrol actions only in the body of stomach. However, in the discussion they state that alpha1-adrenergic receptors and K-ATP channels are implicated in the effects of these phytoestrogens in the "gastrointestinal" smooth muscle, suggesting that the same intracellular pathways are also involved in the intestine. Several abbreviations are not explained in full in the text: SR: sarcoplasmic reticulum, ER: estrogen receptor, NDP: nucleotide diphosphates. Authors state that "SQ22536, an inhibitor of cAMP synthesis, partially inhibited the resveratrol and genistein action. This finding suggests that resveratrol and genistein may prevent the cAMP signal system and affect the subsequent strength of gastrointestinal contractions" However, with this results I understand that resveratrol and genistein was acting through the cAMP pathway. Could you clarify this point? Conclusion: Authors stated: "and also involved in Ca²⁺ influx inhibition through L-type Ca²⁺ channel". Although Ca²⁺ enters the cell mainly through this type of channel, specific blockers against L-type Ca²⁺ channels were not used in this study. Thus, this sentence should be avoided. Bibliography: Several references are in different styles: References 9, 14 and 22: only the initials of authors' names are showed. Reference 2: authors' names are in capital letters. Figure legends: Legend from Fig 1: Is "B" antrum of stomach and "C" duodenum? Legend from Fig 5: "A" and "B" do not appear in Fig 5. Figures: Figs 3 and 4: Symbols used for statistical significance are confusing. Why are not used always the same symbols to show statistical significance for the effect of genistein and resveratrol against the control values (*