

Re: Manuscript 41644

Dear Editor,

Thank you very much for favourable comments obtained from your reviewers. Please find an enclosed revised version of our manuscript fully prepared according to the comments of your reviewers.

The following comments were given by the reviewers:

Reviewer 0326127

Conclusion: Minor revision

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

1) This is a well designed, performed and written research paper on an actual topic. I have found few errors and want to present few remarks only. 2) For a general reader, it can be important to clarify, how the cecums were assessed at a long-term period? Did you perform relaparotomy? (I think, yes). Please note this in the text. 3) How many animals died from peritonitis during the experiment in different groups? 4) Figure 3: in a Legend, you have explained all abbreviations under columns except "B" (apparently, it was BPC 157). 5) Why did you use letters B and C for your figures (e.g., not traditional A and B)? 6) There are some inaccuracies in References 5 and 37. To be corrected. 7) I think, your amount of self-citations is excessive (even taking into account the fact that your team wrote most of the work on BPC 157).

Reviewer 01213231

Conclusion: Accept (General priority)

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

I READ THIS INTERESTING PAPER: THE STUDY WAS WELL CONDUCTED, SCIENTIFIC METHODOLOGY WAS RIGOROUS, THE PROBLEM OF THE PAPER IS THAT ENGLISH IS NOT FLUENT AND SOMETIMES NOT VERY CLEAR, SO THE TEXT RESULTS DIFFICULT TO READ. THERE ARE MANY STUDIES ON BPC-157 THAT SHOWED TO BENEFIT IN INTESTINAL ANASTOMOSIS AND WOUNDS IN RATS AND READING THESE PAPERS I HOPE IT WILL HAVE A POSITIVE IMPACT EVEN IN HUMANS FOR CLINICAL APPLICATION.

To the comments given by the reviewers, see our arguments:

1) This is a well designed, performed and written research paper on an actual topic.

Ad 1. We appreciate this point of the reviewer.

I have found few errors and want to present few remarks only.

- 2) For a general reader, it can be important to clarify, how the cecums were assessed at a long-term period? Did you perform relaparotomy? (I think, yes). Please note this in the text.

Ad 2. Acknowledged (see Materials and methods)

- 3) How many animals died from peritonitis during the experiment in different groups?

Ad 3. Acknowledged. It was indicated that no lethal outcome of the rats with perforated cecum was noted (see Results, concluding sentence).

- 4) Figure 3: in a Legend, you have explained all abbreviations under columns except "B" (apparently, it was BPC 157).

Ad 4. Acknowledged and corrected.

- 5) Why did you use letters B and C for your figures (e.g., not traditional A and B)?

Ad 5. Instead of traditional A and B, etc., we used B and C to directly indicate BPC 157 (B) and control (C) and clearly emphasized the obtained improvements. These clarifications were now carried consistently in the figures text.

- 6) There are some inaccuracies in References 5 and 37. To be corrected.

Ad 6. Acknowledged and corrected.

- 7) I think, your amount of self-citations is excessive (even taking into account the fact that your team wrote most of the work on BPC 157).

Ad 7. We appreciate this point of the reviewer. However, it should be noted that this is the first study describing the direct effect of the agent's application on vascular recruitment and activation toward the perforated defect, and all consequences thereof. There are vessels quickly propagating toward the defect at the caecum surface, defect contraction, bleeding attenuation, MDA- and NO-levels in colon tissue at 15 minutes, and severity of colon lesions and adhesions at 1 and 7 days. In general, their extent would explain the extent of the used literature. Besides, this study of the perforated cecum appears as a direct consequence of our previous studies, in particular, those presented in Word Journal of Gastroenterology (recovery of ischemic/reperfusion colitis) and Vascular Pharmacology (recovery of the inferior caval vein occlusion syndrome), and thereby all these studies merit to be mentioned to give an adequate insight to the readers. And finally, the corresponding studies by other groups, those about cytoprotection, cecum research, and BPC 157 research and effects, are also included in this manuscript. So, we hope that the reviewer will accept our arguments.

Summarizing, we hope that the comments given by the reviewers were satisfactorily replayed. The language edition is also already done. We strongly believe that the reviewer truthfully predicted that this manuscript, when presented in WJG, will have a significant impact for further clinical application.

Sincerely

Predrag Sikiric, MD, PhD
Professor