

July 10.2014

Dear Editor,

Please find enclosed the edited manuscript entitled “ Hormonal protection in acute pancreatitis by ghrelin, leptin and melatonin” ,

authors: Jolanta Jaworek and Stanislaw J. Konturek

for **World Journal of Gastroenterology**.

ESPS Manuscript NO: 9936

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

Reviewer I

I would like to thank for valuable comments, which improved the quality of manuscript.

1. English evaluation of manuscript has been performed by native English speaker and errors were corrected.
2. According to the suggestion of reviewer three figures have been combined in one, and all informations have been placed on this figure.
3. The title is too general - The title of paper has been changed to “ Hormonal protection in acute pancreatitis by ghrelin, leptin and melatonin”
4. Full names has been written as they appears first in the text, and then abbreviations were used (f. ex. Nitric oxide synthase (NOS), nitric oxide (NO). Abbreviations have not been used for words that are used once (f.ex catalase, enteroendocrine cells etc).
5. References have been checked: periods have been placed after last authors, journals names have been changed to italic, ref 8 - name of author (Hegyí), ref.22(now 21), ref. 65, 69, 72, 73, 79, 118 (now -115), 127 (now - 126) have been corrected.
6. Errors have been corrected: Working title is corrected to : Hormones and acute pancreatitis, page 6 -“ grelin” has been changed to “ghrelin”, page 14 -“nothing” to “noting”, “mieloperoxidase” to “myeloperoxidase”.
7. Figure 1 “glucocorticoides” - to “glucocorticoids” , “neutrophiles” to “neutrophils”.
- 8.

Reviewer II

I appreciate very much the positive reviewer’s opinion on the manuscript.

1. Clinical trials - Melatonin has been used in clinical trials in patients with IBD, GERD, gastric ulcers, depression or cancer, but not in these with acute pancreatitis. As far as I know ghrelin or leptin have not been employed in such trials.

2. Reference list has been reduced to 126 cited papers (previously was 134). However, according to the suggestion of one of reviewers, the reference list has been completed with four additional positions.

Reviewer III

I would like to thank for your valuable comments and remarks, which help to improve the quality of manuscript.

1. The number of references has been reduced.
2. Ghrelin producing cells - information was completed on page 5. " The main source of ghrelin in the organism of rats and dogs appears to be X/A cells, whereas in humans ghrelin has been found in P/D1cell type".
3. Des-acyl ghrelin (page 6) - according to the suggestion of Reviewer the part of text concerning des-acyl ghrelin was completed and the recent data from new publications, concerning the biological effects of des-acyl ghrelin have been included (Inoue Y 2013, Shimada T 2013, Delhanty PJ 2012, Pei XM 2014). Above papers have been put into the list of references (ref no - 26-29).
4. Ghrelin and acute pancreatitis (page 7) -number of cited references concerning NF- κ B, have been corrected (to no 44 and 45).
5. Figure 1 - glucocorticoides has been corrected to - glucocorticoids, one of IL-1beta has been removed, IL-6 has been placed on the Fig. 1.

Minor corrections:

1. English evaluation of manuscript has been performed by native English speaker and errors were corrected.
2. Working title - corrected to "Hormones and acute pancreatitis"
3. Page 4 - "...inbalance..." was corrected to "...imbalance..."
4. Page 6 and 7 - "grelin" was corrected to "ghrelin", "...both form of ghrelin..." to "...both forms of ghrelin...", "...glucogenesis..." to "...neoglucogenesis...", "Anti-inflammatory effects of ghrelin has been shown" to "Anti-inflammatory effects of ghrelin have been shown ..."
5. Page 6 - the sentence was corrected to ". Both GHS-R1s have been expressed mainly in the pituitary, but these receptors have also been detected in the pancreas, spleen, heart..."
6. Page 7 - "...leukemi..." to "...leukemic...", "...MAPK-1 phosphatase..." to "...MAPK phosphatase-1..."
7. Page 7 - the sentence has been changed to : "The anti-inflammatory effect of ghrelin could also be attributed to the activation of NOS and to enhanced production and release of NO"
8. Page 8 "...acelerated..." - "...accelerated..."
9. Page 11 "... might prevents..." to "...might prevent..."

10. Page 12. "...is not paralleled..." to "...are not parallel...", " Results of above studies leads to the conclusion..." to " The results of above studies lead to the conclusion.... ", "Nevertheless..." to "Nevertheless...", "...interleukin production to combat with pathogens..." to "...interleukin production to combat pathogens..."
11. Page 13 "...harderian gland..." to "...Harderian gland..."
12. Page 14 "...NF-kappaB..." to "...NF-κB..."
13. Page 15 "Melatonin act as direct and indirect antioxidant..." to "Melatonin works as direct and indirect antioxidant ...",
14. Page 16 "Melatonin slow down the activity of macrophages..." to "Melatonin slows down the activity of macrophages..."
15. Figure 1 legend "...calcitonin gene-related peptide ..." to "... calcitonin gene-related-peptide...", "...glutathione ..." to "...glutathione ...", "...superoxide dysmutase ..." to "...superoxide dismutase..."

Thank you very much for publishing our paper in the World Journal of Gastroenterology.

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