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RE:

**Title:** Novel methylxanthine derivative-mediated anti-inflammatory effects in inflammatory bowel disease.

**Authors:** Lee IA, Kamba A, Low D, Mizoguchi E

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

**ESPS Manuscript NO:** 5852

Dear Editor,

Thank you for informing us that this review article will be required minor revisions. We have read the reviewers' comments with interest, and we are glad that all reviewers recommend this manuscript for publication. According to the suggestion by reviewers 2 and 3, we have shortened this manuscript by reducing 1,700 words and 17 references. In addition, the format of the manuscript has been updated in accordance to editorial suggestions.

We hope that the revised manuscript is now suitable for the publication in WJG. If you have any questions, please feel free to contact me.

Sincerely yours,

Emiko Mizoguchi, M.D., Ph.D.

**Point-by-point responder reviewers' comments**

**Reviewer #1 (02445239):**

Nice review article covering all available hitherto details the treatment modality of IBD in concise manner

We greatly appreciate this comment.

**Reviewer #2 (00504725):**

Would consider shortening manuscript

According to the suggestion, we have shortened this manuscript by reducing 1,700 words including 16 references.

**Reviewer #3 (00505024):**

1) This is an interesting review paper. It summarizes that methylxanthine derivatives, chitinase 3-like 1 in particular, as potential targets for treating inflammation and inhibiting carcinogenesis in IBD. The subject matter is novel, evidence and reasoning are supportive. Minor suggestions: 1, on page 7 and 8 or other pages as well, it is important to not describe caffeine, theophylline and pentoxifylline as “strong” or “potent” or etc.

Thanks for this important advice. We have removed the speculative words without any evidence including “strong” and “potent” from this manuscript.

2) On pages 9-12, when talking about PDE subtypes and adenosine receptors, please only focus on those that moderate inflammation. Other contents are not relevant and distract readers.

We greatly appreciate the above comment. According to this suggestion, we have only focused on the anti-inflammatory effects of PDE subtypes and adenosine receptors in this manuscript.