

Dear editor:

Thank you for your thorough review and salient observations. We have carefully read and addressed the comments from reviewers in the revised manuscript. Please see the point-by-point responses. All the changes are highlighted and we hope the revised manuscript is suitable for publication in World J Gastroenterol.

Best regards,

Sincerely,

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Response for reviewer 1:

COMMENTS TO AUTHORS

Dear Author(s) The manuscript is presented in an easy understandable manner. The topic in the manuscript is very well explained. But it requires substantial corrections for the acceptance. A. General suggestions/corrections/comments 1. Grammar corrections and spacing mistakes all over the manuscript were highlighted in the text needs to be corrected. 2. Technical corrections are highlighted in the text. B. Materials and Methods 1. Only female rats were taken not male and comparison between the two could have been made. 2. Disease activity index needs to be modified in the text with clear explanation or presented in the table format as below. Scoring of the disease activity index (DAI) [Chen et al., 2007] Score Decrease in growth (%) or Weight loss Stool consistency Occult/gross rectal bleeding 0 0 Normal Normal 1 1~5 Normal Occult blood + 2 5~10 Loose stools

Occult blood ++ 3 10~15 Loose stools Occult blood +++ 4 >15 Diarrhea Gross bleeding C.

Discussion 1. Concise the text. Do not exceed more than 2 printed pages. D. References 1. Morris et al., - not included in the reference part 2. Follow the journal format in the reference part. Check the authors instruction section for the format. 3. Citation of too many references in the manuscript should be avoided. E. Suggestions: The following reports can also be considered which would further help in discussing the results. Satish Kumar CS, Kondal Reddy K, Reddy AG, Vinoth A, Ch SR, Boobalan G, Rao GS (2015) Protective effect of Lactobacillus plantarum 21, a probiotic on trinitrobenzenesulfonicacid-induced ulcerative colitis in rats. *Int Immunopharmacol.* 25(2): 504-10. Gopu B, Dileep D, Rani MU, Kumar CS, Kumar MV, Reddy AG. (2015). Protective role of curcumin and flunixin against acetic-acid induced IBD via modulating inflammatory mediators and cytokine profile in rats. *J Environ Pathol Toxicol Oncol.* 34(4): 309-20. Fujiwara D, Chen L, Wei B, Braun J. (2011). Small intestine CD11c+ CD8+ T cells suppress CD4+ T cell-induced immune colitis. *Am J Physiol Gastrointest Liver Physiol.* 300(6):G939-G47. Rutella S, Locatelli F. (2011) Intestinal dendritic cells in the pathogenesis of inflammatory bowel disease. *World J Gastroenterol.* 17(33):3761-75. Notes: Chen Y, Si J, Liu W, et al. 2007. Induction of experimental acute ulcerative colitis in rats by administration of dextran sulfate sodium at low concentration followed by intracolonic administration of 30% ethanol. *Journal of Zhejiang University Science B.* 8(9):632-637.

Response:

COMMENT 1. Grammar corrections and spacing mistakes all over the manuscript were highlighted in the text needs to be corrected.

Response: Thank you for your review. We invited the language polishing company (MedSci(code: 1802-9DC0-06A3-DCBF-4ACE) to edit our manuscript. Maybe, there are many grammatical errors in the article, so we had edited the full text again by MedSci.

COMMENT 2. Technical corrections are highlighted in the text.

Response: Thank you for your guidance. All technical corrections had been highlighted in our article. You can find them in the present revised manuscript.

COMMENT 3. 3.1. Only female rats were taken not male and comparison between the two could have been made. 2. Disease activity index needs to be modified in the text with clear explanation or presented in the table format as below. Scoring of the disease activity index (DAI) [Chen et al., 2007]

Score	Decrease in growth (%)	Weight loss	Stool consistency	Occult/gross rectal bleeding
0	0	Normal	Normal	0
1	1~5	Normal	Occult blood	+
2	5~10	Loose stools	Occult blood	++
3	10~15	Loose stools	Occult blood	+++
4	>15	Diarrhea	Gross bleeding	

Response: Thank you for your guidance. 3.1 Many previous reports had indicated that female or male rats (mice) were used to induce experimental colitis. To eliminate the difference of data, we select male mice to induce experimental colitis. The same model of colitis were used in many our previous study (Zhao, et al; Front. Pharmacol. 2016, 7(11) 1-11.). 3.2 According to your guidance and the article of Chen et al, scoring of the disease activity index (DAI) was shown in the table 1. You can find it in the page 39, line 1-2.

COMMENT 4. CDiscussion 1. Concise the text. Do not exceed more than 2 printed pages.

Response: Thank you for your guidance. To explain our present results, we detailedly indicated experimental results, the pathogenesis of TNBS-induced colitis and inflammatory bowel disease (IBD), the role of CD8⁺CD11c⁺ cell in IBD, and the mechanism of Curcumin (Cur) via many references. According to your suggestion, we had concised the present discussion. However, the discussion part still exceeds more than 2 printed pages. So hope you can give us a chance. Thank you very much.

COMMENT 5. References 1. Morris et al., - not included in the reference part 2. Follow the journal format in the reference part. Check the authors instruction section for the format.

Response: Thank you for your criticism. We had revised “Morris” to “Salaga”. And according to the WJG format to check and revise the whole manuscript. You can find them in the revised manuscript.

COMMENT 6. 3. Citation of too many references in the manuscript should be avoided. E. Suggestions: The following reports can also be considered which would further help in discussing the results. Satish Kumar CS, Kondal Reddy K, Reddy AG, Vinoth A, Ch SR, Boobalan G, Rao GS (2015) Protective effect of Lactobacillus plantarum 21, a probiotic on trinitrobenzenesulfonic acid-induced ulcerative colitis in rats. Int Immunopharmacol. 25(2): 504-10. Gopu B, Dileep D, Rani MU, Kumar CS, Kumar MV, Reddy AG. (2015). Protective role of curcumin and flunixin against acetic-acid induced IBD via modulating inflammatory mediators and cytokine profile in rats. J Environ Pathol Toxicol Oncol. 34(4): 309-20. Fujiwara D, Chen L, Wei B, Braun J. (2011). Small intestine CD11c⁺ CD8⁺ T cells suppress CD4⁺ T cell-induced immune colitis. Am J Physiol Gastrointest Liver Physiol. 300(6):G939-G47. Rutella S, Locatelli F. (2011) Intestinal dendritic cells in the pathogenesis of inflammatory bowel disease. World J Gastroenterol. 17(33):3761-75. Notes: Chen Y, Si J, Liu W, et al. 2007. Induction of experimental acute ulcerative colitis in rats by administration of dextran sulfate sodium at low concentration followed by intracolonic administration of 30% ethanol. Journal of Zhejiang University Science B. 8(9):632-637.

Response: Thank you for your guidance. (1) To explain our present results, we detailedly indicated experimental results, the pathogenesis of TNBS-induced colitis and inflammatory bowel disease (IBD), the role of CD8⁺CD11c⁺ cell in IBD, and the mechanism of Curcumin (Cur) via many references. (2) According to your suggestion and the above references, we selected the part references, used them in our article, and inserted in the reference part. You can find them in the page 33, line 9-12, and page 34, line 11-13. Especially, the article of Chen et al. we think it is

very important to explore DAI, so we cited it in the present study. So, you can find it in page 12, line 19-20, and page 32, line 11-15.

Response for reviewer 2:

COMMENTS TO AUTHORS

Please check the English ("is a transmembrane protein I which") Abstract: - define all abbreviations used in this section (see DAI) - be more specific ... what "significantly decrease" means Statistical analysis: - scores are by definition qualitative ordinal data so the correct summarization is done using medial and (Q1-Q3) while the comparisons are conducted with non-parametric tests instead of parametric (ANOVA). Results: - use boxplot with median and Q1-Q3 instead of column charts. - the results are presented for 10 animals per group while in the material and methods is written that 8 animals per group were used. Conclusion: - "we demonstrated that Cur effectively treated experimental colitis, which was realized by inhibiting CD8 + CD11c + cells". No such demonstration was presented in the manuscript.

Response: Thank you for your guidance. We had checked the whole article, and define all abbreviations used in the abstract. You can find them in page 6, line 13-14, 17, and line 22-23. And we revise "significantly" into "obviously", you can find it in page 6, line 18. In the statistical analysis, we had added the analysis of nonparametric data. You can find it in page 15, line 16-17. We think that column chart is an effective formation presented data which was widely used in many previous studies. In present study, we assuredly used 8 mice per group. And we had revised it. You can find it in page 40, line 9. Our conclusion were presented respectively in page 7, line 3-4, page 16, line 22-24, page 17, line 1-6, page 18, line 2-10, page 19, line 1-10, page 22, line 12-24, page 23, line 1-12, in the manuscript. If it is still error in this manuscript, please you give me a chance to revise it again, thank you very much.

Response for reviewer 3:

COMMENTS TO AUTHORS

Method of induction of colitis by the using agent and its dose should be mentioned (oral or intraperitoneal)



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Response: Thank you for your guidance. The method of induction of colitis by the using agent and its dose was described in page 11, line 8-21. Experimental colitis was induced by 100 mg / kg TNBS via enema.