

Format for ANSWERING REVIEWERS

July 10, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 18305-Review.doc).

Title: Role of peroxisome proliferator-activated receptors alpha and gamma in gastric ulcer: An overview of experimental evidences

Author: Lekha Saha

Name of Journal: *World Journal of Gastrointestinal Pharmacology and Therapeutics*

ESPS Manuscript NO: 18305

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

Reviewed by 00012309

| | |
|--------------------------|--|
| Manuscript Number | 18305 |
| Manuscript Title | <u>Role of Peroxisome Proliferator-Activated Receptors alpha and gamma in gastric ulcer: an overview of experimental evidences</u> |
| Review Time | 2015-05-27 22:36 |

| | |
|----------------------------|---|
| Comments To Authors | Well written paper. The authors are certainly aware that PPR-gamma behaves in the colon as a potent differentiating agent, its expression being maximal at crypt base, to only cease while moving to the crypt head. Mesalamine, its perfect pharmacological ligand, seems to exert its anti-inflammatory and anti-cancer activity in IBD thanks to its ability to bind and activate PPR-gamma. Could the authors envisage and speculate on any link or implications of these colon facts with their gastric findings ? |
| Classification | <input type="checkbox"/> Grade A (Excellent) <input checked="" type="checkbox"/> Grade B (Very good) <input type="checkbox"/> Grade C (Good) <input type="checkbox"/> Grade D (Fair) <input type="checkbox"/> Grade E (Poor) |
| Language evaluation | <input checked="" type="checkbox"/> Grade A: priority publishing <input type="checkbox"/> Grade B: minor language polishing <input type="checkbox"/> Grade C: a great deal of language polishing <input type="checkbox"/> Grade D: rejected |
| Conclusion | <input checked="" type="checkbox"/> Accept <input type="checkbox"/> High priority for publication <input type="checkbox"/> Rejection <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision |

Response to the comments:

Regarding the anti-inflammatory and anti-cancer activity of PPAR gamma agonist in our

study:- We have demonstrated the antigastric ulcer activity of bezafibrate, PPAR α agonist, in our laboratory. Keeping in view the diversity of defensive mechanisms, the present study was limited to exploring the involvement of mucosal oxidant system, apoptotic pathway and nitric oxide pathway in the mechanism of antigastric ulcer effect of bezafibrate. To explore the nitric oxide mechanism, a nitric oxide synthase inhibitor, N^{ω} -nitro-L-arginine (LNNA) was used. The following parameters were measured: Ulcer Index, Histopathological scoring of gastric ulcer, gastric juice analysis, Gastric mucosal lipid peroxidation parameters, Estimation of nitric oxide metabolite in blood, mRNA expression of iNOS and cNOS enzyme in gastric mucosa and Gastric mucosal DNA fragmentation study. Bezafibrate demonstrated dose-dependent antiulcer activity, showed antisecretory and gastro protective action, reduced lipid peroxidation, inhibit iNOS expression, preserve cNOS expression and qualitatively inhibited DNA fragmentation and improved upon the Histopathological score of gastric mucosa.

The histopathological findings of the gastric mucosa: Aspirin administration showed superficial erosion and ulceration on the mucosa and infiltration of inflammatory cells. Co administration of bezafibrate with aspirin showed gastric mucosa with reepithilization, formation of pits and decreased infiltration of inflammatory cells. From this finding we can say that bezafibrate (a PPAR alpha agonist) might have anti inflammatory activity in gastric ulcer

Reviewed by 02458583

| | |
|-------------------|---|
| Manuscript Number | 18305 |
| Manuscript Title | Role of Peroxisome Proliferator-Activated Receptors alpha and gamma in gastric ulcer: an overview of experimental evidences |
| Review Time | 2015-06-16 05:12 |

| | |
|---------------------------------|---|
| Comments To Authors | - |
| Classification | <input type="radio"/> Grade A (Excellent) |
| | <input type="radio"/> Grade B (Very good) |
| | <input type="radio"/> Grade C (Good) |
| | <input type="radio"/> Grade D (Fair) |
| | <input type="radio"/> Grade E (Poor) |
| Language evaluation | <input type="radio"/> Grade A: priority publishing |
| | <input type="radio"/> Grade B: minor language polishing |
| | <input type="radio"/> Grade C: a great deal of language polishing |
| | <input type="radio"/> Grade D: rejected |
| Conclusion | <input type="radio"/> Accept |
| | <input type="radio"/> High priority for publication |
| | <input type="radio"/> Rejection |
| | <input type="radio"/> Minor revision |
| | <input type="radio"/> Major revision |
| Upload Required Documents | |
| Confidential Comments To Editor | |

Comments To Authors

There was no comments to the authors by reviewer no 02458583