1 COMMENTS TO AUTHORS

In the study mycophenolic acid (MPA) and the prodrug mycophenolate mofetil (MMF) were investigated concerning its therapeutic and toxic effects. The prodrug with D-glucosamine (MGLS) was found with a 68 percent release. A decrease of the activity score was found. The topic is highly specialized.

Comments 1. Is there any data about TNF-alpha or IL-1beta levels available?

Answer: Sorry this data is not available presently with us.

2. The TNBS model is well established. Do the authors have any data about MGLS in the transfer model or others?

Answer: the codrugs have been screened in TNBS-induced experimental colitis model presently. The synthesized prodrugs are being screened in T cell transfer model in mice, the data of the same will be communicated in our upcoming publication.

2 COMMENTS TO AUTHORS

The authors used mycophenolic acid (MPA); an immunosuppressant and its morpholinoethyl ester prodrug being mycophenolate mofetil are under investigation for the treatment of IBD. The authors focus on synthesizing colon- targeted prodrugs wherein MPA was bio-reversibly linked with N-sugars to mask carboxyl group of MPA responsible for GI side effects. The authors have been successful in showing using data a significant mitigating outcome on TNBS- induced colitis in Wistar rats compared to MPA. The manuscript is very dense and rich of several methods, but the quality of the microphotographs is poor and needs to be improved.

Answer: quality of the microphotographs has been improved. Photomicrographs with better resolution have been provided in ppt slide as per editor's suggestion.

3 COMMENTS TO AUTHORS

The results is very interesting and the paper is overall well written. I have several comments.

In the Introduction the available IBD therapy is not explained in detail. We have many other therapeutic options except aminosalycilates.

Answer: A paragraph on available IBD therapy and recent developments in therapeutic options for IBD have been included in the revised paper.

Furthermore, it is not clear why the new co-drugs are more effective than mycophenolic acid.

Answer: New co-drugs are more effective than MPA because:

1. Synthesized prodrugs are colon- targeting in nature which have delivered MPA to the site of action i. e. colon in effective concentration. Orally administered plain MPA is absorbed in the upper GIT readily that is why only a small fraction of the administered dose reaches the distal part of the GIT i.e. colon hence its efficacy is less as compared to codrugs
2. Aminosugars glucosamine and galactosamine have been conjugated with MPA using codrug approach. Colon-specific activation of these codrugs released MPA and aminosugars in colon which would have helped in retaining architecture of mucin and forming protective layer on the mucosa of colon. In addition to this, polyhydroxy

nature of these aminosugars helped in increasing hydrophilicity of MPA to such an extent that absorption of the intact prodrug in upper GIT was minimized that assured efficient delivery to colon.

3. Aminosugars have significantly added to the mitigating effect of MPA.
4. This reasoning has been mentioned under section of "discussion" on page 12 and page 16."