

DDS-induced colorectal fibrosis in mice: anti-fibrotic effects of GED 0507-34 levo, a novel PPAR γ ligand

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Intestinal fibrosis is a progressive process characterized by de novo synthesis and uncontrolled deposition of extracellular matrix components (ECM) following a tissue chronic inflammation mainly regulated by Transforming Growth Factor (TGF) β /Smads pathway. Frequently associated to Inflammatory Bowel Disease (IBD), intestinal fibrosis may lead to stenosis and obstructions that require surgery up to 75% of patients as drugs currently used in IBD are unable to improve fibrostenosis lesions (1). Peroxisome proliferator-activated receptor (PPAR)- γ is able to antagonize (TGF) β /Smads and could be an crucial target to develop novel antifibrotic therapeutic strategies (2).

Aim of this study is to evaluate the antifibrotic action of a novel PPAR γ agonist, GED 0507-34 levo, in colonic fibrosis in mice.

Immunohistochemistry and immunoblotting evaluations, TGF β 1, CTGF, Collagen types I-III, Smad3, α -SMA, were performed in in three groups of C57BL/6 mice: Dextran Sulphate Sodium (DSS) colitis group, DSS+GED group and controls.

Evident macroscopic and microscopic lesions in the most of colons of DSS treated mice were observed compared to DSS+GED mice and controls. The tissue levels of the main markers of fibrosis resulted significantly increased in DSS mice and restored by administration of GED.

GED seems to prevents ECM colonic deposition and to improve the intestinal fibrotic lesions by its ability in controlling TGF β /Smads pathway signalling activation.

References

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Keywords

Inflammatory Bowel Disease, animal model, fibrosis, TGF β /Smads, PPAR γ .