

## Anti-fibrotic effect of a novel PPAR- $\gamma$ ligand, GED-0507-34 LEVO, in DSS induced colonic fibrosis in mice

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Intestinal fibrosis is a common complication of inflammatory bowel disease (IBD) in which chronic inflammation leads to abnormal deposition of extracellular matrix components (ECM) causing obstruction and loss of function of the intestinal tract involved (1). Fibrogenesis is mainly regulated by transforming growth factor (TGF)  $\beta$ /Smad pathway and a key antagonist of this signaling is represented by peroxisome proliferator-activated receptor (PPAR)- $\gamma$ . As the anti-inflammatory drugs currently used in IBD are unable to improve intestinal fibrosis the exploration of new therapeutical approaches has now become crucial (2). Aim of this study is to evaluate the antifibrotic action of a novel PPAR $\gamma$  agonist, GED-0507-34-LEVO (GED), in colon fibrosis in mice.

Chronic colitis and fibrosis were induced in C57BL/6 mice by administration of 2,5% (w/v) dextrane sulphate sodium (DSS) in drinking water for 5 days followed by 7 days of water for 3 cycles. Mice were divided into 3 groups: DSS, DSS+GED and control. 30mg/Kg/mice of GED was daily administered by oral gavage starting from the second DSS cycle. Samples from colon were excised and processed to assess macroscopic lesions, histological and morphometrical aspects and immunohistochemical and immunoblotting analysis for TGF $\beta$ 1, CTGF, collagen types I-III, Smad3,  $\alpha$ -SMA.

Evident shortening and dilation in the most of colons of DSS treated mice were observed. Macroscopic and microscopic findings were significantly improved in DSS mice+GED compared with control mice. The tissue levels of collagen and  $\alpha$ -SMA, specific markers of fibrosis, resulted significantly increased in mice receiving DSS compared to control mice, as well as the expression of TGF $\beta$ 1, CTGF, Smad3. DSS+GED group showed reduced expression of all markers involved.

GED significantly improves the intestinal fibrotic lesions in DSS chronic colitis murine model and controls the pivotal molecular events leading to fibrosis.

### References

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### Key words

Animal models, Intestinal Fibrosis, TGF $\beta$ 1/Smads.