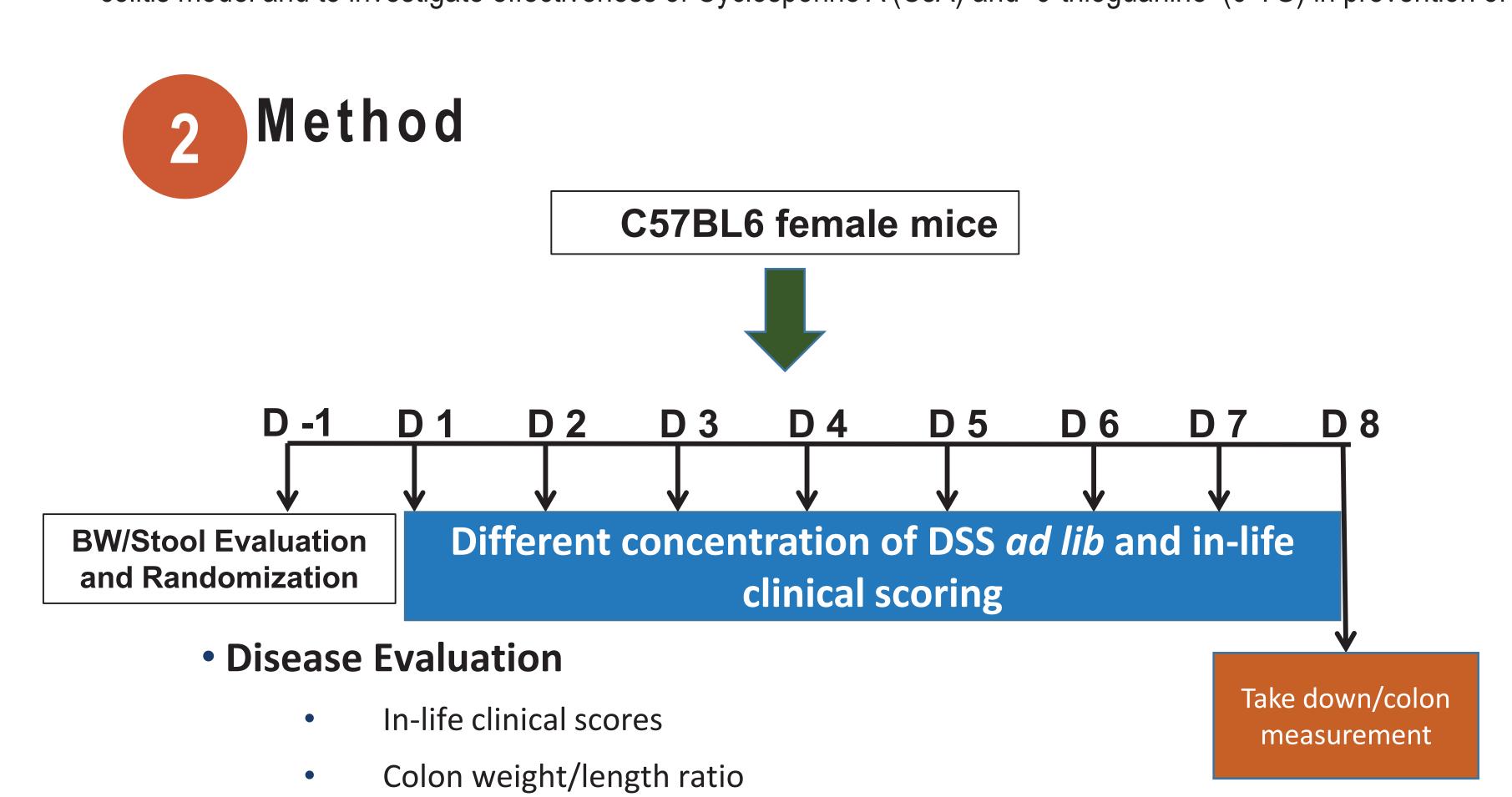
Cyclosporine A (CsA) partially prevents progression of Colitis in an acute DSS-induced mouse model

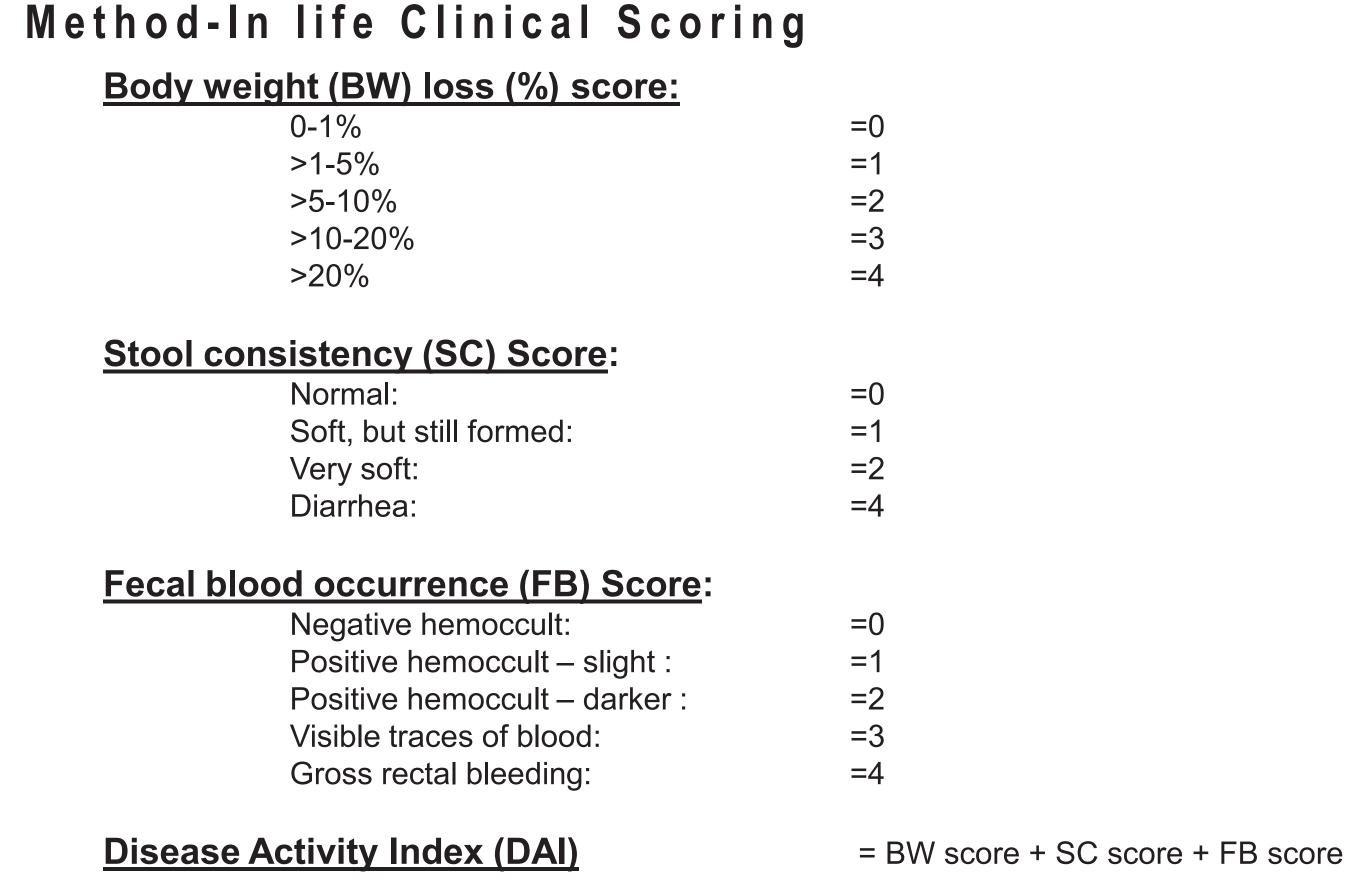
charles river

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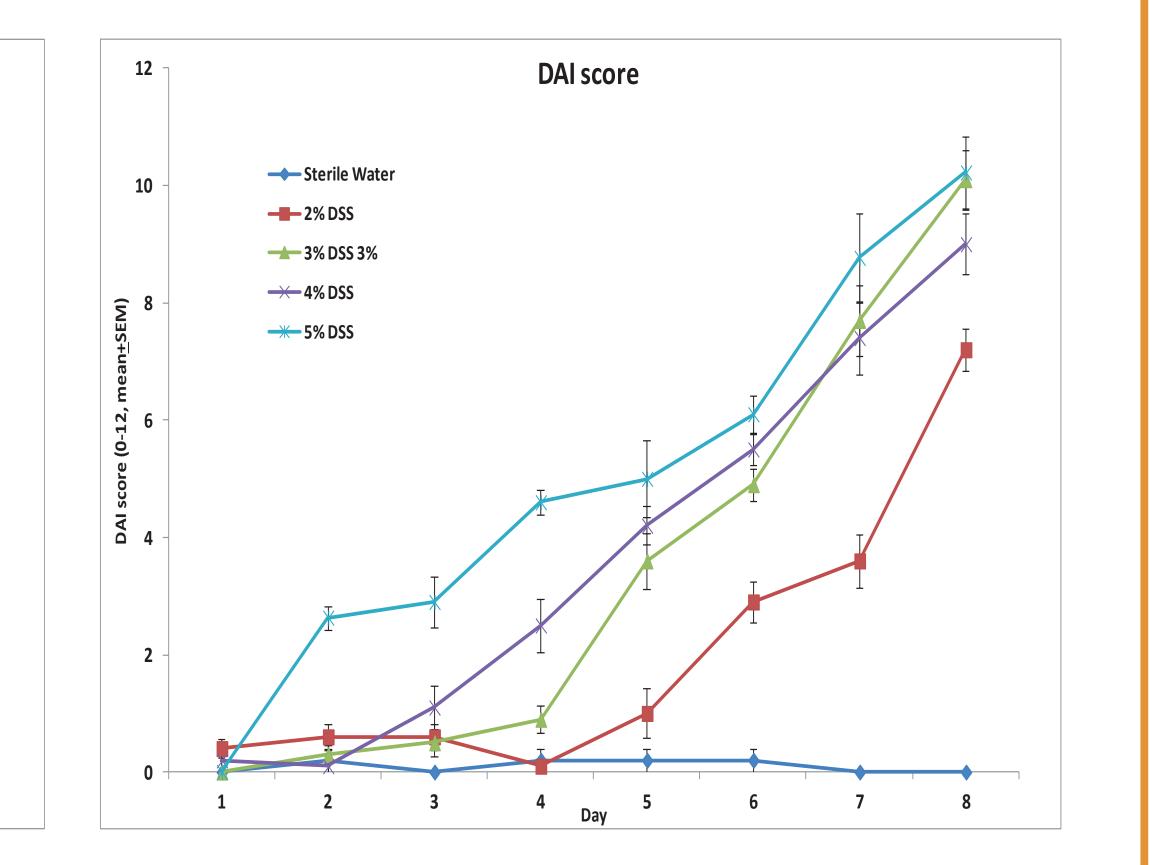
Among the various animal models of inflammatory bowel disease (IBD), the chemically-induced colitis models are the most common due to their robustness, reproducibility and overall etiology of the disease with some resemblance to the human disease. Among various chemically induced colitis models, the dextran sulfate sodium (DSS)-induced colitis model is widely used because of its simplicity and many similarities with human ulcerative colitis. We conducted a study to establish a relevant colitis model and to investigate effectiveness of Cyclosporine A (CsA) and 6-thioguanine (6-TG) in prevention of the disease.



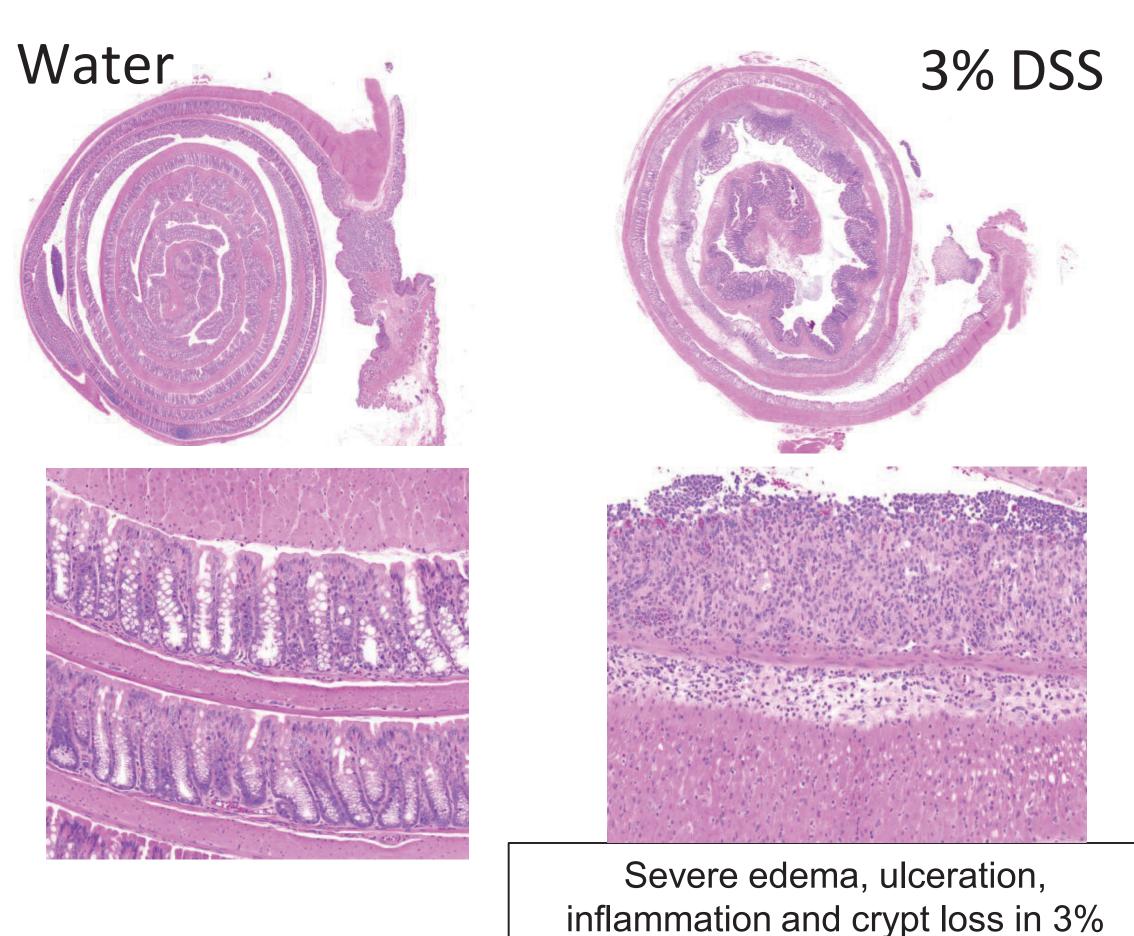












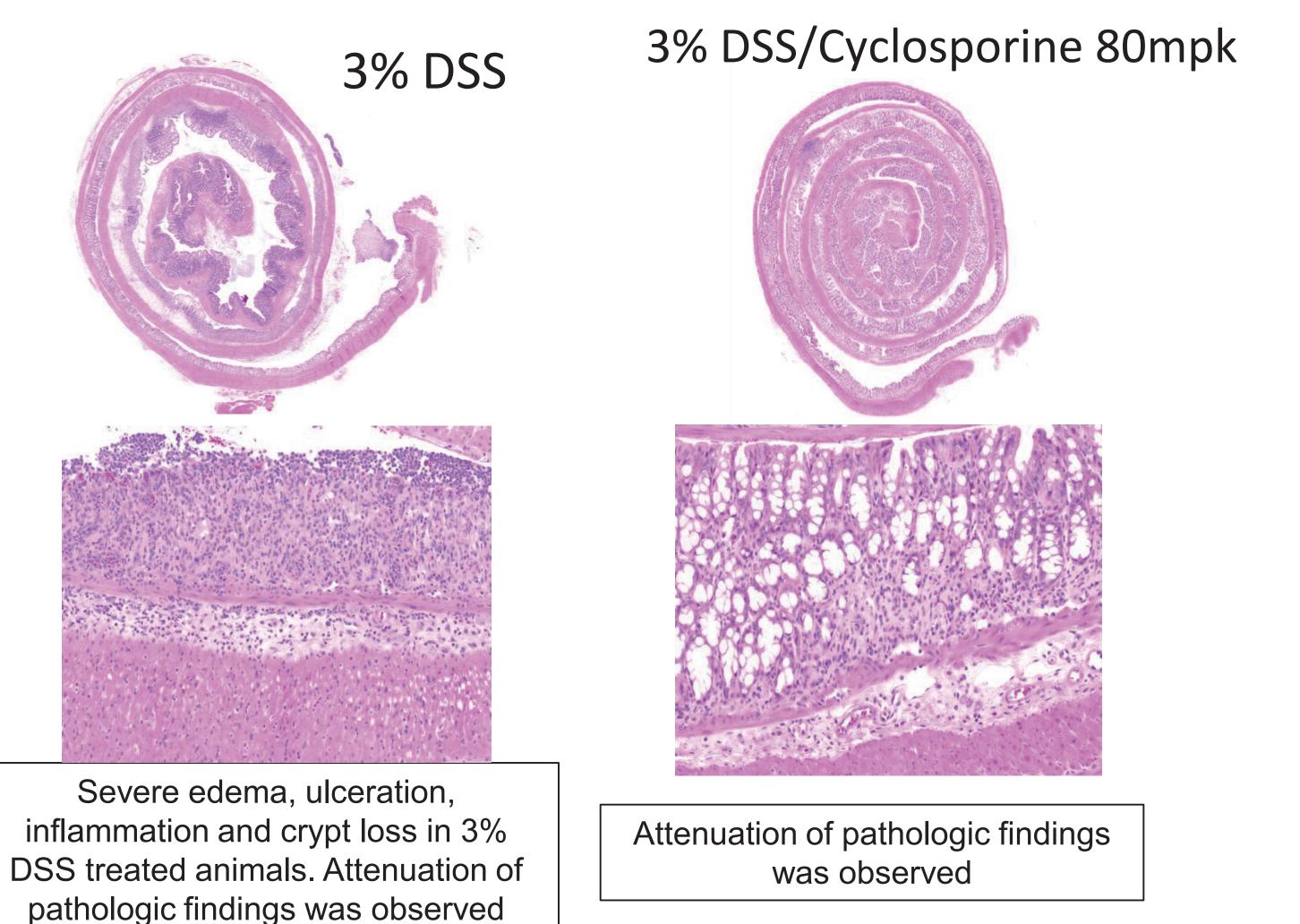
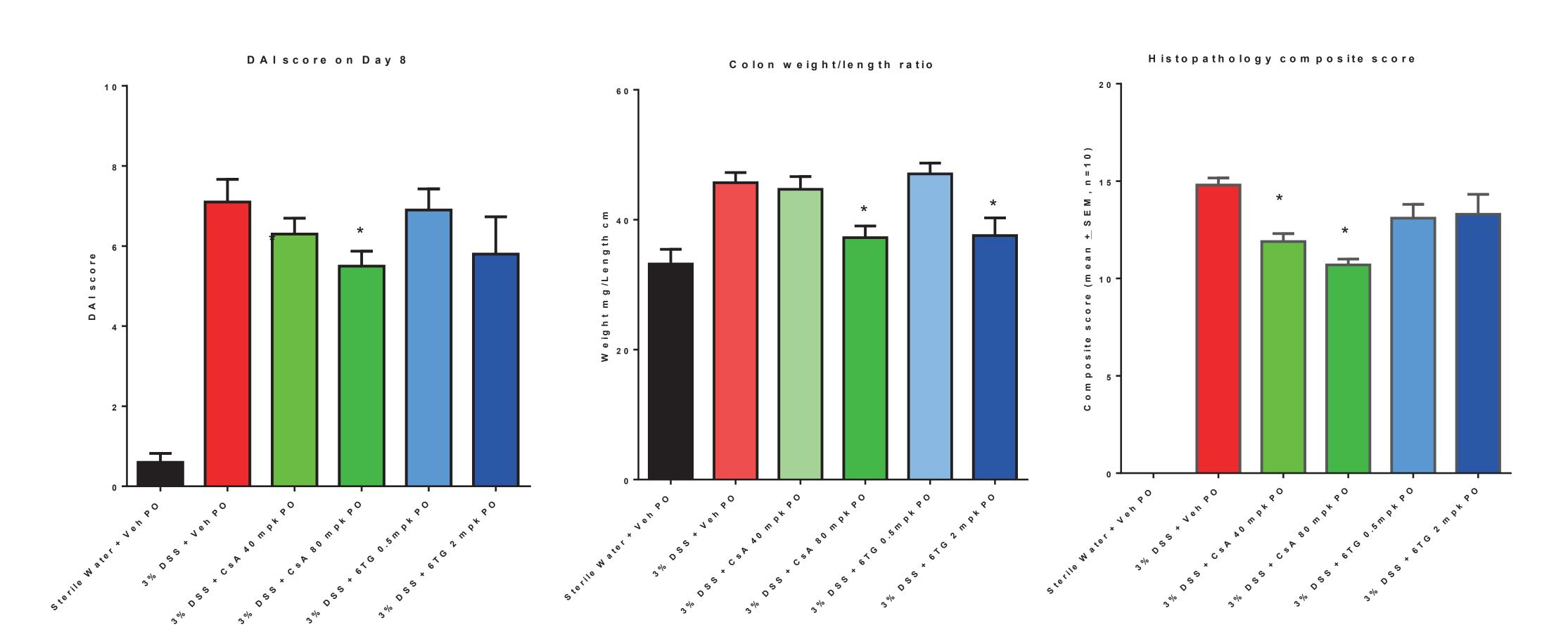


Figure 3: Effects of Cyclosporine A (40 & 80 mpk), and 6-TG (0.5 & 2 mpk) on acute DSS colitis



*Significantly different from group 2 p≤0.05



Results:

- 1. Ad libitum administration of DSS in drinking water induced dose-dependent decreases in body weight and clinical scoring (Figure 1). Severe weight loss and few unscheduled euthanasia was seen with 4% and 5% DSS. Diarrhea and occult blood in stools were evident by Day 2 in 5% DSS group, at Days 3-4 in the 3% and 4% DSS groups and at Day 5 in the 2% DSS group (data not shown)
- 2. Colon length shortened and weight increased in DSS-treated mice (Data from 3% DSS in figure 3).
- 3. Histopathologically, evidence of colitis (Severe edema, ulceration, inflammation and crypt loss) in colon sections was seen in all groups (representatives from 3% DSS shown in Figure 2).
- 4. 3%DSS was selected as an optimal dose level for disease induction and was used to investigate efficacy of CsA.
- 5. At 40 mg/kg and to a greater extent at 80 mg/kg, CsA reduced both in-life and microscopic disease severity (Figure 3). 6-TG had no meaningful effect on histology findings or body weight (figure 3).

Conclusions: Ad libitum administration of DSS in drinking water induced dose-dependent colitis in mice as assessed by in-life clinical signs and histopathological evaluation. Overall, results show that 3% DSS in drinking water was optimal for colitis induction in these mice. Furthermore, CsA can partially prevent disease progression and at appropriate dose levels can be used as a positive control for screening of anti-IBD compounds.