

# Anti-inflammatory Effect of Extract of *Terminalia Sericea* Roots in an Experimental Model of Colitis

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Sericoside is a traditional herbal saponin from *Terminalia sericea* (Family: Combretaceae). We studied the anti-inflammatory effect of sericoside on acute inflammatory colitis induced by ethanolic 2,4,6-trinitrobenzene sulfonic acid in male rats. Intestinal mucosa lesions were judged by their macroscopic damage score and measuring by myeloperoxidase (MPO) activity. Pretreatment of sericoside (30 mg/kg daily by gavage for 10 days) significantly reduced the macroscopic damage score and inhibited MPO activity. These results showed that sericoside attenuated the inflammatory effect and suggested its possible role in treating acute inflammatory diseases such as inflammatory bowel disease.

**Key words**——inflammatory bowel disease, *Terminalia sericea*, sericoside, 2,4,6-trinitrobenzene sulfonic acid, myeloperoxidase

## INTRODUCTION

The leaves and roots of *Terminalia sericea* (Family: Combretaceae) have traditionally been used as a popular folk medicine for treating bacterial infections, diarrhea and diabetes.<sup>1)</sup> Sericoside, the triterpenoidal saponin of *Terminalia sericea* extract, has anti-inflammatory<sup>2)</sup> and antioxidant activities.<sup>3)</sup>

Inflammatory bowel disease (IBD) is an immune-mediated disorder of the gastrointestinal tract characterized by inflammation lesions and ul-

ceration. An experimental model of IBD is known to be induced by 2,4,6-trinitrobenzenesulfonic acid (TNBS). We reported previously that superoxide was generated in TNBS-induced colitis and (–)-epigallocatechin-3-gallate suppressed neutrophil infiltration by decreasing superoxide generation due to its radical scavenging activity.<sup>4)</sup>

In the present study, we investigated the protective effects of sericoside on TNBS-induced colitis in the rat.

## MATERIALS AND METHODS

**Animals**——The animal procedures were reviewed and approved by the Animal Research Committee of Gifu Women's University and the Japanese Government Animal Protection and management Law. Male Sprague-Dawley rats (Charles River Japan, Inc., Kyoto, Japan) weighing 150–175 g were housed in standard plastic cages with food and tap water available *ad libitum*. The animal facility was under a 12/12-hr dark/light cycle, at a constant temperature of 24±2°C and a relative humidity of 60%.

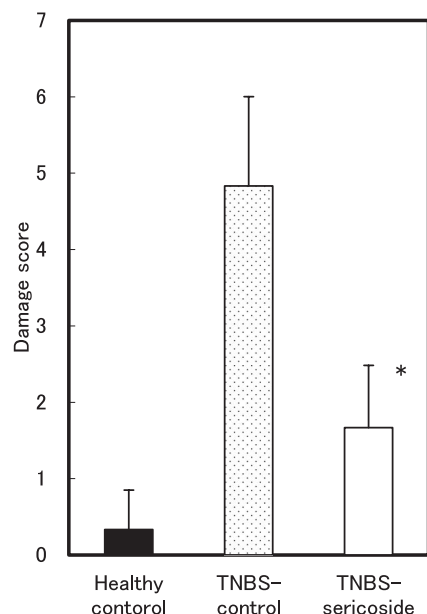
**Drugs and Treatment**——Sericoside was provided by Daiwa Chemical Industries Co. (Tokyo, Japan) and suspended in 0.3% carboxy methyl cellulose and administered daily (30 mg/kg) for 10 days by gavage before colitis induction.

**Colitis Induction**——Colitis was induced as described earlier by rectal intraluminal administration of 120 mg/kg TNBS (Wako Pure Chemicals, Tokyo, Japan) in 50% (v/v) ethanol.<sup>4)</sup>

**Macroscopic Assessment**——Macroscopic damage was assessed by a scoring system taking into account the area of inflammation and the presence or absence of ulcers using four standard parameters.<sup>5)</sup> Adhesions and wall thickness were graded on a scale from 0 to 2. Strictures and ulcers were scored from 0 to 3.

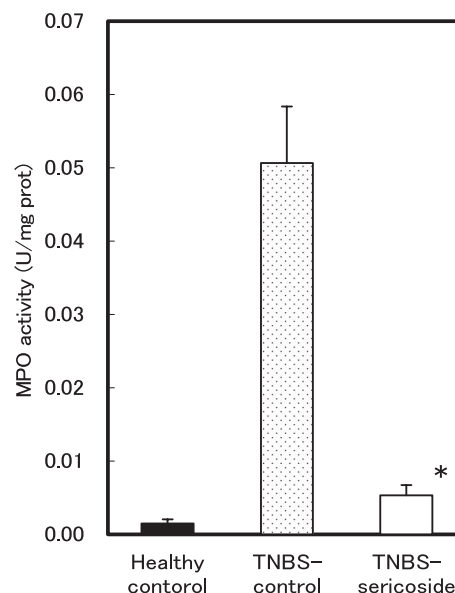
**Myeloperoxidase (MPO) Activity Measurement**——Samples were collected according to a method previously described.<sup>6)</sup> Mucosa was scraped from 5 cm long samples and homogenized in hexadecyltrimethylammonium bromide buffer (pH 6.0). The homogenate was sonicated and subjected to three cycles of freezing and centrifuged for 30 min at 20000 × *g* at 4°C. The aliquot of the supernatant was assayed for MPO activity according to a method previously described.<sup>7)</sup> The rate of change in absorbance was measured at 460 nm

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**Fig. 1.** Effect of Sericoside Treatment on Macroscopic Damage Score in Distal Colon Mucosa

Thirty mg/kg of sericoside was given for 10 days prior to the administration of TNBS-sericoside. Results are presented as the mean ± S.E. of six experiments: \* $p < 0.001$ , compared with the TNBS-control.



**Fig. 2.** Effect of Sericoside on Neutrophil Granulocyte Infiltration into Distal Colon Mucosa

Experimental procedure is described in Fig. 1. Results are presented as the mean ± S.E. of six experiments: \* $p < 0.001$ , compared with the TNBS-control.

in the mixture of supernatant and guaiacol- $\text{H}_2\text{O}_2$  buffer. One MPO activity unit corresponds to 1  $\mu\text{mol}$  of  $\text{H}_2\text{O}_2$  degraded in 1 min. Protein was quantified using a protein assay kit (Pierce, IL, USA).

**Statistics** — Results are expressed as the mean ± S.E. Student's  $t$ -test was used for statistical comparison.

## RESULTS AND DISCUSSION

TNBS induced an ulcerative inflammation of the distal colon characterized by reddish edematous mucosa. Treatment with sericoside resulted in a decrease in the extent and severity of the injury. The severity of colitis was assessed by histological grading of the colitis.<sup>5)</sup> The sericoside pretreated group had lower mean scores than those of the TNBS control group (Fig. 1). These results suggest that sericoside has an anti-inflammatory effect against acute mucosal injury.

Rectal tissue MPO activity, which is a marker of neutrophil infiltration into the mucosa, was significantly increased in the TNBS control group compared with the healthy control group (Fig. 2). Treatment with sericoside significantly inhibited MPO activity by 90% ( $p < 0.001$ ). The anti-inflammatory

effects were due to reduced neutrophil activation.

The superoxide was generated in TNBS-induced colitis.<sup>6)</sup> The water and methanol extract of *Terminalia sericea* has a potent antioxidative effect.<sup>3)</sup> These results suggest that sericoside were effective by reducing neutrophil infiltration and decreasing superoxide generation due to its radical scavenging activity.

The results of this study suggest that administration of sericoside may be therapeutically beneficial for the treatment of IBD in humans.

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