

DA-6034, a New Therapeutic Agent of Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) is a multifactorial disorder with unknown etiology and pathogenesis. DA-6034, 7-carboxymethoxy-3', 4', 5-trimethoxy flavone, is a synthetic derivative of eupatilin that is a flavonoid derivative and main component of the extract of *Artemisiae* species, a Korean folk medicine used in the treatment of chronic diarrhea. This study was performed to evaluate the oral therapeutic effect of DA-6034 in four experimental animal models of inflammatory bowel disease.

Acute chemical colitis was induced by intracolonic instillation of 1.2 ml of 4% acetic acid solution. Prednisolone (1 mg/kg), sulfasalazine (100 mg/kg) and DA-6034 (0.3~3 mg/kg) were orally administered twice daily for 6 days in these rats. Chronic chemical colitis was induced by intracolonic administration of trinitrobenzene sulfonic acid (TNBS) 30 mg in 50% ethanol and these drugs were orally administered for 6 or 20 days. In chemical-induced IBD models, all these drugs reduced the severity of colitis and especially, DA-6034 (3 mg/kg) showed more potent effect than other drugs in macroscopic lesion score. In mice, colitis was induced by administration of 5% DSS solution for 5 days followed by 5 days of plain water. DA-6034 reduced the colitis index-diarrhea incidence, body weight, mortality and intestinal gross lesion. In HLA-B27 transgenic rats, DA-6034 (3 mg/kg) and prednisolone (0.5 mg/kg) were treated orally twice daily for 6 weeks. The HLA-B27 transgenic rats showed only mild colitis, compared with the chemical-induced colitis models. DA-6034 ameliorated the loose stool and decreased microscopic damage, which is the important indicator of this model.

In conclusion, oral therapy of DA-6034 attenuated the macroscopic and histological damages of the colon in all three experimental models of IBD, which suggest that DA-6034 could be a promising drug in the treatment of IBD.