

EFFECTS OF THE NON-PEPTIDYL LOW MOLECULAR WEIGHT RADICAL SCAVENGER IAC IN DNBS-INDUCED COLITIS IN RATS

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Inflammatory bowel disease (IBD), including Crohn's disease and ulcerative colitis, are chronic inflammatory disorders of unknown origin. It is likely that there are multiple factors contributing to IBD, including genetic and environmental factors. Intestinal inflammation is accompanied by excessive production of reactive oxygen and nitrogen radical species due to the massive infiltration of polymorphonuclear and mononuclear leukocytes (1). Recent studies indicate that antioxidant compounds are protective in experimental colitis. There are several experimental models of intestinal inflammation. It has been suggested that the transmural immune activation and inflammation seen in the 2,4 Dinitrobenzene Sulphonic Acid (DNBS) model of colitis resembles that found in Crohn's disease. **Aim:** We investigated the effects of the non-peptidyl, low molecular weight radical scavenger bis(1-hydroxy-2,2,6,6-tetramethyl-4-piperidinyloxy)decandioate (IAC) in the DNBS model of colitis, relying on its high reactivity with most, if not all, oxygen, nitrogen and carbon centred radicals (2). Thanks to its peculiar physico-chemical properties, IAC is also easily distributed in cell membranes and intra-extra cellular compartments. **Methods:** Colitis was induced in male SD rats by intrarectal administration of 15 mg/rat DNBS. IAC (30 mg/kg) was administered daily (orally or i.p.) starting from the day before the induction of colitis for 7 days (n=6-8 per group). Colonic damage was assessed by means of macroscopic and histological scores, myeloperoxidase activity (MPO) and TNF- α tissue levels. **Results:** Colitis impaired body weight gain and markedly increased all inflammatory parameters. IAC significantly counteracted the reduction in body weight gain, decreased colonic damage and inflammation and TNF- α levels in DNBS-colitis.

Treatment	Macroscopic score	Microscopic score	MPO (U/mg)	TNF- α (pg/mg)
Intrarectal DNBS	8.0 \pm 1.1	6.5 \pm 0.5	16.7 \pm 4.9	107.7 \pm 9.2
DNBS+IAC 30 mg/kg os	3.8 \pm 0.6**	3.4 \pm 0.8**	6.1 \pm 2.1*	77.0 \pm 8.1*
DNBS+IAC 30 mg/kg i.p.	3.6 \pm 0.5**	3.5 \pm 0.5**	3.3 \pm 1.0**	76.1 \pm 8.0*

One-way analysis of variance. *p<0.05 vs. DNBS; **p<0.01 vs. DNBS

Conclusions: The antioxidant IAC significantly ameliorates experimental colitis in rats. This strengthens the notion that antioxidant compounds may have therapeutic potential in IBD.

1. Kruidenier L., Kuiper I., Lamers C. and Verspaget H.W. (2003) J. Pathol. 201:28-36.
2. Valgimigli L., Pedulli G.F., Paolini M. (2001) Free Rad. Biol. Med. 31:708-716.

