

APP, A NOVEL SELECTIVE ADENOSINE DEAMINASE INHIBITOR, IS EFFECTIVE AGAINST EXPERIMENTAL COLITIS

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Introduction. Adenosine plays a beneficial role as immuno-modulator in inflamed tissues. On this basis, drugs able to promote the accumulation of endogenous adenosine could represent a novel strategy to treat inflammatory bowel diseases. **Methods.** The effects of APP (novel adenosine deaminase inhibitor), EHNA (reference adenosine deaminase inhibitor) and dexamethasone (DEX) were tested in rats with 2,4-dinitrobenzenesulphonic acid-induced colitis (DNBS, 15 mg/rat), to assess systemic [food intake, body and spleen weight, tumour necrosis factor- α (TNF- α) and interleukin-6 (IL-6) plasma levels] and colonic inflammatory parameters [macroscopic and microscopic damage, TNF- α , myeloperoxidase (MPO) and malondialdehyde (MDA) levels]. DNBS-treated animals received APP (5 mg/kg), EHNA (30 mg/kg), DEX (0.1 mg/kg) or vehicle intraperitoneally for 7 days, starting 1 day before DNBS. **Results.** DNBS caused bowel inflammation and decreased food intake and body weight. Animals treated with APP or EHNA, but not DEX, displayed greater food intake and body weight than inflamed rats. Colitis was associated with an increase in spleen weight, which was counteracted by APP, EHNA and DEX. DNBS-induced colitis was characterized by macroscopic and microscopic tissue alterations. Colonic MPO, MDA and TNF- α levels, as well as plasma TNF- α and IL-6 were increased. These parameters were ameliorated by APP, EHNA or DEX. Data are summarized in table. **Conclusions.** APP exerts significant anti-inflammatory effects on intestinal inflammation reducing pro-inflammatory cytokines and local cellular infiltration. APP might provide the basis for the development of a novel class of drugs active on adenosine pathways and effective against inflammatory bowel disease.

	Macroscopic damage	Microscopic damage	Plasma TNF- α (pg/ml)	Plasma IL-6 (pg/ml)	Tissue TNF- α (pg/100 mg)	Tissue MPO (pg/100 mg)	Tissue MDA (μ M/mg)
Normal	1 \pm 0.6	1.4 \pm 0.3	5 \pm 1.3	122.7 \pm 2.5	3.8 \pm 1.1	3.2 \pm 1.8	148 \pm 23.8
DNBS	7.5 \pm 2	4.3 \pm 1.2	41 \pm 9.4	206.5 \pm 18	8.6 \pm 1.5	17.1 \pm 4.5	548 \pm 23.4
+EHNA	4.6 \pm 1.3	2.8 \pm 0.5	4.9 \pm 1.2	124.7 \pm 10.1	4.9 \pm 1.9	8.1 \pm 1.9	306.6 \pm 29
+APP	4.2 \pm 1.1	2.5 \pm 0.8	5 \pm 1.1	126.3 \pm 12.1	5.3 \pm 1	7.5 \pm 1.3	442.3 \pm 29
+DEX	3.8 \pm 1.6	1.6 \pm 0.9	5.4 \pm 1.5	121.1 \pm 9.3	5 \pm 0.5	7.2 \pm 1.8	234.5 \pm 22