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Beneficial effects of an ellagic-enriched pomegranate extract on chronic TNBS-induced colitis in rats

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Background and purpose: A complex system of intracellular signalling molecules, influences the uncontrolled immune system activation in inflammatory bowel disease (IBD). In previous studies, *Punica granatum* L. (pomegranate) has been shown to exert, antioxidant and anti-inflammatory effects. Besides, we have documented that Ellagic Acid (EA), a natural polyphenol compound present in pomegranate, decreased the degree of inflammation associated with chronic experimental colonic inflammation. To study the effects of a dietary EA-enriched pomegranate extract (PE) in a murine chronic model of CD. Experimental approach: Colonic injury was induced by intracolonic instillation of trinitrobenzenesulphonic acid (TNBS) (30mg/rat). Male Wistar rats were fed with diets : (1) standard diet (n=10), (2) PE 250 mg/kg/day (n=10) , (3) PE 500 mg/kg/day (n=10), (4) EA 10 mg/kg/day (n=10) and (5) EA 10 mg/kg/day enriched- PE 250 mg/kg/day (n=10) during 30 days before TNBS instillation and 2 weeks before killing. Inflammation response was assessed by MPO activity and TNF-α production. iNOS, COX- 2, p38, JNK, p-ERK1/2 MAPKs , IKBα inhibitory protein, and nuclear p65 NF-κB expressions were studied by western blotting in colon mucosa. The statistical significance was evaluated by one-way analysis of variance (ANOVA). Key results: MPO activity and the TNF-α levels were significantly reduced in dietary fed rats after TNBS administration (Table 1). Diets drastically decreased COX-2 and iNOS overexpression, reduced MAPKs activation, prevented the inhibitory protein (IκB-α) degradation as well as induced the nuclear p65 NF-κB downregulation. Conclusions and implications: Dietary supplementation of EA contributes in the beneficial effect of PE in this experimental colitis model and may be a novel therapeutic strategy to manage IBD.

Table 1

Group	n	MPO (U/mg tissue)	n	TNF-α (pg/mgtissue)
Sham	10	0.51 ± 0.1	10	5.8 ± 0.9
TNBS	10	$2.57 \pm 0.2^{***}$	10	$14.7 \pm 1.5^{***}$
PE 250	10	$1.32 \pm 0.19^{++}$	10	$7.90 \pm 0.84^{++}$
PE500	10	$1.40 \pm 0.14^{+++}$	10	$6.70 \pm 0.80^{+++}$
EA 10	10	$1.05 \pm 0.2^{+++}$	10	$9.3 \pm 0.93^{+}$
PE+EA	10	$0.78 \pm 0.19^{+++}$	10	$8.6 \pm 0.3^{++}$

*** P<0.001, significantly different from Sham

$^+$ P<0.05, $^{++}$ P<0.01 and $^{+++}$ P<0.001, significantly different from TNBS.