

Polyphenols with anti-inflammatory activity in the gastrointestinal tract

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Polyphenols, e.g. flavonoids, anthocyanins, tannins, constitute one of the largest groups of plant secondary metabolites, recognized for their diverse functions *in planta* and impact on human nutrition and health. Among polyphenols, ellagitannins (ETs) have been found in many edible fruits such as raspberry, strawberry, cranberry, pomegranate, and nuts. Although preliminary data indicate a high potential as a new class of compounds with interesting applications for human health, the biological effects of ellagitannins need to be further elucidated.

The gastrointestinal tract represents an important barrier between the human hosts and microbial populations. One potential consequence of host-microbial interactions is the development of mucosal inflammation, which can lead to gastritis and ulcer. It has been demonstrated that gastric epithelial cells, after *H. pylori* infection, show higher levels of cytokines including IL-1 β , IL-6, TNF- α , and IL-8, a potent neutrophil-activating chemokine that plays a central role in gastric diseases (Crabtree et al., 1993; Crabtree et al., 1995). This response depends on activation of NF- κ B and the early-response transcription factor Activating Protein-1 (AP-1) (Yasumoto et al., 1992). ETs have shown anti-inflammatory and anti-*Helicobacter pylori* properties; however their anti-inflammatory activity at gastric level was not previously investigated. The aim of the study was to evaluate the effects of ETs from *Rubus* berries on gastric inflammation. Ellagitannin enriched extracts were prepared from *Rubus fruticosus* L. (blackberry) and *Rubus idaeus* L. (raspberry) (Gasperotti et al., 2010). The *in vitro* anti-inflammatory activity was tested on human gastric cell line AGS stimulated by TNF- α and IL-1 β for evaluating the effect on NF- κ B driven transcription, nuclear translocation and IL-8 secretion. Our data show that ETs were able to inhibit TNF- α induced NF- κ B driven transcription and nuclear translocation. ETs also inhibited IL-8 secretion induced by TNF- α and IL-1 β at very low concentrations (0.5-4 μ g/mL). Sanguin H-6 and lambertianin C, the major ETs present in the extracts, were found to be responsible, at least in part, for the effect of the mixtures.

The protective effect of ETs was evaluated on ethanol-induced gastric lesions in rats. Rats were treated orally for ten days with 20 mg/kg/day of ETs, and ethanol was given one hour before the sacrifice. Gastric mucosa was then isolated and used for the determination of Trolox equivalents, superoxide dismutase and catalase activities, and IL-8 release. *In vitro*, ETs of blackberry and raspberry decreased Ulcer Index by 88% and 75% respectively and protected from the ethanol induced oxidative stress in rats. CINC-1 (the rat homologue of IL-8) secretion in the gastric mucosa of ethanol-treated rats was reduced in the animals receiving blackberry and raspberry ETs. The results of the present study report for the first time the preventing effect of ETs in gastric inflammation and support for their use in dietary regimens against peptic ulcer.

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