

# Anti-inflammatory activity of *Vitis vinifera* L. leaves water extract: effect of the *in vitro* gastro-intestinal digestion

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Botanicals are widely consumed all over the world for health purposes, with increased usage in the general population, in many different types of products, including foods, and plant food supplements (PFS). Several reports support for the beneficial effects of botanicals against gastro-intestinal inflammation. Gastrointestinal inflammatory diseases are emerging pathological conditions whose prevalence has increased in the last few years; these pathologies, including inflammatory bowel diseases (IBD) in the gut and gastritis and ulcer in the stomach, are strictly connected to the westernization of lifestyle and industrialization. At the molecular level, both gastric and intestinal inflammatory processes are characterized by an increased secretion of the chemokine IL-8 from epithelial layer, mostly mediated by the activation of the NF- $\kappa$ B pathway (Crabtree et al., 1995; Wang et al., 2009). Recently, a consumer survey evaluating the usage of PFS across six European countries, reported *Vitis vinifera* L. in the top list among PFS ingredients and at fifth position in Germany (Garcia-Alvarez et al., 2014). Previous results obtained in our laboratory demonstrated the anti-inflammatory activity of an aqueous extract from *Vitis vinifera* L. dried leaves in two *in vitro* models of gastric (AGS) and intestinal (Caco-2) inflammation. However, gastrointestinal digestion process occurring after oral consumption of PFS could alter the amount and, consequently, the biological activity of the extract. The aim of this work was to establish how the biological activity of a red vine leaves extract changed before and after *in vitro* gastric or gastro-intestinal digestion, focusing on IL-8 secretion and promoter activity as molecular targets.

The extract was subjected to *in vitro* gastric or gastrointestinal digestion; then, it was characterized by a validated HPLC-DAD method and tested on human epithelial gastric (AGS) and intestinal (Caco-2) cells. Our results showed that the water extract from red vine leaves inhibited TNF $\alpha$ -induced IL-8 secretion and expression (IC<sub>50</sub> 56.8 and 9.5  $\mu$ g/mL, respectively) in human gastric epithelial cells and that the effect should be maintained, although to a lesser extent, after gastric digestion (IC<sub>50</sub> 97.9 and 43.4  $\mu$ g/mL on the IL-8 secretion and expression respectively). On the contrary, the effect after intestinal digestion was dramatically decreased since degradation of the active components in the gut did not allow the extract to efficiently counteract TNF $\alpha$  or IL-1 $\beta$ -induced IL-8 expression and NF- $\kappa$ B pathway. The main molecular target of the vine leaves extract at the gastric level included TNF $\alpha$ -induced activation of NF- $\kappa$ B (IC<sub>50</sub> 17 and 23.5  $\mu$ g/mL on the NF- $\kappa$ B driven transcription and traslocation respectively) and occurred at concentrations easily reachable after PFS consumption based on red vine leaves water extract as ingredient. Our findings suggest that PFS containing water extracts from *Vitis vinifera* L. leaves could be useful to attenuate gastric inflammation inhibiting IL-8 secretion and expression through impairment of the NF- $\kappa$ B pathway.

Crabtree et al. (1995). *J. Clin. Pathol* 48: 41-45.

Garcia-Alvarez et al. (2014). *PLoS One* 9: e92265.

Wang et al. (2009). *Cell Mol Immunol* 6: 327-34.