

Protective Effect of Gut Phenolic Metabolites Against Inflammation and Atherosclerosis: an in vitro Approach

Cristian Del Bo', Mirko Marino, Lorenzo Battisti, Alessandro Moreletti, Marisa Porrini, Salvatore Ciappellano.

Objective: Vascular inflammation is characterised by an increase in the expression of vasoconstrictor factors (e.g. cytokines, interleukins, cell adhesion molecules) and a decrease of vasodilator agents such as nitric oxide. This event induces endothelial dysfunction that seems to be the first step in atherosclerosis development. Accumulating evidence suggests that polyphenols, and their metabolic products, may play a beneficial role in attenuating inflammation and atherosclerosis even if their mechanism of action is still unrevealed.

The study aims to evaluate the capacity of gut phenolic metabolites such as protocatechuic, gallic, and vanillic acid (PA, GA, VA, respectively) to decrease the adhesion of monocytes (THP-1) to endothelial cells (HUVECs), in a stimulated pro-inflammatory environment and to reduce the production of cell adhesion molecules (VCAM-1 and E-selectin), as potential markers involved in such modulation.

Methods: The adhesion of labelled THP-1 cells to HUVECs was promoted by tumor necrosis factor α (TNF- α ; 100 ng mL⁻¹). Successively, HUVECs were incubated with different concentrations (from 0.01 to 10 μ g mL⁻¹) of PA, GA and VA for 24 h. The adhesion process and the levels of vascular cell adhesion molecules (VCAM-1 and E-selectin) were measured. Data were analysed by one-way analysis of variance (ANOVA)

Results: Preliminary experiments have shown the capacity of PA and GA to reduce THP-1 adhesion to HUVECs at 1 μ g mL⁻¹ (-29.5%; $p < 0.05$ and -23.6%; $p < 0.001$, respectively) and 10 μ g mL⁻¹ (-44.3%; $p < 0.01$ and -27.8%; $p < 0.001$, respectively), while VA only at the maximum concentration (-20.8%; $p < 0.005$). The supplementation with phenolic metabolites decreases the levels of E-selectin but not VCAM-1.

Conclusions: In conclusion, these preliminary results support the capacity of gut phenolic metabolites to reduce THP-1 adhesion to HUVECs and decrease the production of E-selectin. Further experiments are ongoing to identify the mechanisms of action of each compound involved in the anti-atherosclerotic activity.