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PUNICA GRANATUM-DERIVED EXTRACELLULAR VESICLES EFFECTS ON AN IN VITRO GASTROINTESTINAL BARRIER MODEL OF INTESTINAL INFLAMMATION

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Vegetables and fruit-derived extracellular vesicles have been proposed as a potential nanomedicine for intestinal disorders; however, their impact on intestinal barrier integrity in gut inflammation has not been explored yet. It is widely known that a diet rich of fruits and vegetables preserves the integrity of the intestinal epithelial barrier, avoiding inflammatory stimuli and contributing to maintain a "healthy gut". The ability to transport bioactive molecules and the low toxicity give the vesicles a remarkable versatility in the field of nutritional science. These findings challenge the classical view of dietary bioactive compounds as freely dissolved small molecules, suggesting instead that a significant fraction of plant bioactivity may be organized within membrane-enclosed nanostructures whose biological effects depend not only on their molecular cargo but also on the architectural properties of the vesicle itself.

This study aimed to evaluate Punica granatum (pomegranate)-derived EVs on an in vitro gastrointestinal (GI) barrier model of intestinal inflammation through cytokine gene expression evaluation with RT-qPCR. We have preliminary set a GI barrier in vitro model by using Caco-2, HT29, and Raji B cells co-cultured on filter cell culture chamber inserts (Transwell with porous 0.4-um-sized polycarbonate filters); then, barrier was exposed to an inflammatory stimulus (dextran-sulfate sodium salt (DSS) and TNF-α) before or after EVs administration. A morphometric characterization, via Cryo-TEM, DLS, and NTA analyses, revealed pomegranate juice-derived particles concentration, shape and diameter; the HPLC ESI/MS-TOF analysis was used to determine the EVs cargo.

Pomegranate-derived EVs are biocompatible and exert both antioxidant and anti-inflammatory properties as well as protection on epithelial tight junction functionality upon internalization, visualized by confocal microscopy, demonstrating a stronger beneficial effect on intestinal mucosa than juice soluble bioactive molecules.