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**Supplementation with a pomegranate extract abrogates hypercholesterolemia-induced coronary endothelial dysfunction in mice**

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**Purpose:** Epidemiological studies support an inverse correlation between polyphenol-rich food consumption and coronary artery disease mortality. Potential cardiovascular protective effects of polyphenol-rich food juices and extracts have been reported in recent years. Yet the mechanisms involved remain largely unknown. We sought to investigate whether supplementation with a pomegranate extract rich in punicalagins (Pomaron®, POX) would render beneficial effects on coronary vasomotion and cell function, characterizing the underlying mechanisms, in a clinically-relevant experimental model.

**Methods and results:** Pigs (n=24) were fed during 10 days a normocholesterolemic (NC) or a Western-type hypercholesterolemic (HC) diet. Half of the NC and HC animals were provided a supplement of 625 mg/day POX (200 mg/punicalagins day; NC=POX and HC=POX). Coronary responses to escalating-doses of vasoactive agents were analyzed. POX supplementation in dyslipidemic animals prevented diet-induced impairment of endothelial relaxation, reaching vasodilatory values comparable to those found in NC animals, upon stimulation of muscarinic receptors or with A23189. These POX-related beneficial effects were associated with vascular Akt/eNOS activation, and lower levels of MCP-1. POX supplementation reduced systemic oxidative stress (high HDL antioxidant capacity and higher LDL resistance to oxidation) and coronary vascular DNA damage. All NC animals displayed a similar vasodilatory dose-response effect to SNP. L-NMMA blunted all vasorelaxation responses except for exogenous NO donation.

**Conclusions:** POXsupplementation prevents hypercholesterolemia-induced coronary endothelial dysfunction by activating the Akt/eNOS pathway and favorably counteracting vascular inflammation and oxidative DNA damage. | BENCH

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**Fasting triglyceridemia influences postprandial endothelial response to a single Mediterranean-type meal compared to a high-saturated fat meal**

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Endothelial dysfunction is considered a precursor of atherosclerosis and is an independent predictor of cardiovascular events. A high-saturated fat meal (HSFAM) has been shown to induce postprandial endothelial dysfunction. However, no studies have evaluated the acute endothelial effect of a single mixed Mediterranean-type meal (MMM). Our aim here was to evaluate the postprandial endothelial and metabolic function in response to MMM in comparison to an isocaloric HSFAM and explore the role of baseline triglyceridemia. In this crossover study, 28 healthy non-smoking males were randomly assigned two isocaloric meals on two separate mornings. The MMM, consisting of salmon, almonds and vegetables baked in olive oil, provided 51% of total calories from fat (7.67g SFA and 2.29g of omega-3) while the HSFAM, consisting of sausage, egg and cheese sandwich and fried potatoes, provided 98% of total energy from fat (14.79g SFA). Endothelial function was evaluated by brachial artery flow-mediated dilation (FMD) after a 12-hour fast (T0) and four hours after consumption of the meals. Fasting and postprandial plasma fatty acid profiles were also evaluated. Postprandial FMD was significantly reduced by the HSFAM (-2.5±5.3%, p=0.004), while it was not influenced by the MMM (-1.21±4.6%, ns). Postprandial insulin, AUC TG, TG:HDL, and CHD:HDL were increased to a greater degree in response to the HSFAM. Plasma enrichment in omega-3 PUFA (EPA, DPA and DHA) at the expanson of SFA (18%) was observed following the MMM. Furthermore, postprandial FMD was significantly altered among individuals with fasting TG levels above the group median (0.87 mmol/L). A single MMM exert no deleterious effect on postprandial endothelial function and has a lesser impact on metabolic profile than does a HSFAM. This could be resulting from significant postprandial enrichment in fatty acids with better endothelial properties. Moreover, even slightly elevated but normal fasting triglyceridemia could increase the risk of endothelial injury following a single HSFAM.