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## THE ACTION OF NUTRACEUTICALS ON KEY MACROPHAGE PROCESSES ASSOCIATED WITH ATHEROSCLEROSIS

**Objectives:** To investigate the actions of nutraceuticals on key macrophage processes associated with atherosclerosis.

**Background:** Atherosclerosis is an inflammatory disorder of the vasculature orchestrated by the action of cytokines. Macrophages play a pivotal role in atherosclerosis and represent promising therapeutic targets. Current therapies against atherosclerosis are associated with substantial residual risk together with other issues such as adverse side effects. In addition, there have been numerous disappointments on many pharmaceutical agents identified from drug discovery programs. This has initiated interest in nutraceuticals as preventative or therapeutic agents in atherosclerosis but requires an in-depth understanding of their actions. The purpose of this study was to delineate the effects of nutraceuticals on key macrophage processes associated with atherosclerosis together with the molecular mechanisms underlying their actions.

**Methods:** The studies used a combination of macrophage cell lines and primary cultures. Gene expression was monitored by real time quantitative PCR and western blot analysis. The production of reactive oxygen species was determined using a kit from Abcam. Foam cell formation was monitored by uptake of fluorescently labeled modified LDL, intracellular lipid profile and cholesterol efflux. Inflammasome activation was evaluated by following the release of interleukin (IL)-1beta. Cell viability was assessed by release of lactate dehydrogenase.

**Results:** The studies focused on key components in olive oil and omega-6 polyunsaturated fatty acids. These attenuated the expression of key markers of inflammation induced by several pro-atherogenic cytokines, the uptake of modified LDL, macropinocytosis and foam cell formation in macrophages. In addition, they stimulated macrophage cholesterol efflux. A differential effect was observed for other parameters such as production of reactive oxygen species and production of IL-1beta via inflammasome activation. The mechanisms underlying such actions will be presented.

**Conclusions:** The studies provide novel insights into the actions of nutraceuticals on key macrophage processes associated with atherosclerosis.