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NUTRACEUTICALS IN THE PREVENTION AND TREATMENT OF ATHEROSCLEROSIS

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Objectives: To investigate the effects of nutraceuticals on key processes associated with atherosclerosis *in vitro* and *in vivo*.

Background: Atherosclerosis is an inflammatory disease of the vasculature in which macrophages play key roles at all stages and represent promising therapeutic targets. Unfortunately, current therapies against atherosclerosis are not fully effective and associated with other issues such as adverse side effects. In addition, there have been many failures on pharmaceutical agents identified from drug discovery programs. Nutraceuticals represent promising alternatives in the prevention and treatment of atherosclerosis but requires a thorough understanding of their actions together with the underlying mechanisms. The purpose of this study was to address this with emphasis on key macrophage processes associated with atherosclerosis.

Methods: A combination of macrophage cell lines and primary cultures were used with gene expression analysed by atherosclerosis profiler arrays and real time quantitative PCR. Foam cell formation was investigated by following the uptake of fluorescently labeled modified LDL, intracellular lipid profiling and cholesterol efflux assays. Inflammasome activation was evaluated by following the release of interleukin (IL)-1beta using an ELISA and ROS production using a kit from Abcam. The effects in vivo were analysed in C57BL/6 mice fed a high fat diet.

Results: The studies focused on polyphenols, flavanols and omega-6 polyunsaturated fatty acids. These either inhibited or had no effect on several key macrophage processes associated with atherosclerosis such as pro-inflammatory gene expression, the uptake of modified LDL, macropinocytosis, ROS production and the activation of the inflammasome. In addition, where analysed, the nutraceutical inhibited several atherosclerosis-associated markers in mice fed a high fat diet. The mechanisms underlying such actions will be presented.

Conclusions: The studies provide new insights into the beneficial actions of nutraceuticals in atherosclerosis.