Purification of PEIPC, an important oxidized phospholipid in the development of cardiovascular disease

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Abstract

Cardiovascular disease is the leading cause of death worldwide, claiming more than 17 million lives every year. The direct and indirect costs of which total more than $320.1 billion. In order to treat this growing disease, it is of the utmost importance to determine the exact mechanism by which oxidized lipids in LDL stimulate endothelial cells, the first step in fatty streak formation, initial lesions in atherosclerosis. The oxidized phospholipid of particular interest to us is 1-palmitoyl-2-(5,6-epoxyisoprostane E2)-sn-glycero-3-phosphocholine, or PEIPC. It is the most active lipid in oxidized LDL with respect to chronic inflammation, with about 80% overlap of the genes regulated by both oxidized LDL and PEIPC. Preliminary results suggest that it is the binding of PEIPC to one of three candidate proteins: EP2, VEGFR2, and GRP78 that causes the stimulation of endothelial cells, potentially triggering the development of lesions, which may lead to heart attack or stroke. So far, GRP78 appears to be the most involved of these three proteins. In order to continue running tests to observe activity and develop a better understanding, we must improve our process of PEIPC purification through chromatography. In the course of my work I was able to make successful improvements of the purification of PEIPC using solid phase extraction, closely monitoring the separation with mass spectrometry. Successful purification of this important lipid is essential for future studies of the biological pathways that lead to atherosclerosis in endothelial cells.