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Ascochlorin Suppresses oxLDL-induced MMP-9 Expression by Inhibiting the MEK/ERK Signaling Pathway in Human THP-1 Macrophages

Jeong Han Kang[1,2], Won-Hwan Park[2], June-Ki Kim[2],
Kwan-Kyu Park[1] and Young-Chae Chang[1]*

[1]*Department of Pathology, Catholic University of Daegu School of Medicine, Daegu 705-718, Korea*
[2]*Cardiovascular Medical Research Center, Dongguk University, Kyungpook 780-714, Korea*

The critical initiating event in atherogenesis involves the invasion of monocytes through the endothelial walls of arteries and the transformation of monocytes from macrophages into foam cells. Also, monocytes/macrophages produce the 92 kDa matrix metalloproteinase-9 (MMP-9) that may contribute to the extravasation, migration and tissue remolding capacities of the phagocytic cells. Here, we investigate the effect of ascochlorin (ASC) on oxLDL-induced MMP-9 expression and activity in human THP-1 macrophages. ASC reduced oxLDL-induced MMP-9 expression and activity. Also, an analysis of MMP-9 activity using pharmacologic inhibitors showed that ASC inhibits MMP-9 activity via the extracellular signal-regulated kinase1 and kinase2 pathways. Our results suggest that ASC may be useful as a potent clinical antiatherogenic agent.

Key words: Ascochlorin, atherosclerosis, MMP-9, activator protein-1

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Expression of PAI-1 is Regulated through the EGFR and MEK/ERK in Rat Kidney Fibroblast

Hyun-Ji Cho, Sung-Young Kim[1] and Young-Chae Chang*

Department of Pathology, Catholic University of Daegu School of Medicine, Daegu 705-718, Korea
[1]*Department of Food Science, Andong Science College 496, Kyo-ri, Seohu-myon, Andong, Kyongbuk 760-822, Korea*

Fibrosis within glomerulosclerosis and between tubulointerstitial fibrosis causes the progressive loss of renal function that leads to end-stage renal disease in humans with diabetes, glomerulonephritis or hypertension. TGF-β1 is the most important profibrotic cytokine in the process of fibrosis. TGF-β1 induces the synthesis of PAI-1 that normally is not present which play important role in fibrosis. In this study, we evaluated that the antifibrotic effect of ascofuranone (AF). Thus, We demonstrated that AF markedly blocks TGF-β1-meidated fibroblastic activation of renal fibroblast cells and, AF suppress TGF-β1-induced fibroblastic activation by reduction of PAI-1 through the inhibition of EGFR and Ras/Raf/MEK/ERK.

Key Wrods: Renal fibrosis, TGF-β1, epidermal growth factor receptor (EGFR), PAI-1