Protective effect of α-lipoic acid on oxidized low density lipoprotein-induced human umbilical vein endothelial cell injury

Yan-Xia Liu, Guo-Zhu Han, Tao Wu, Peng Liu, Qin Zhou, Ke-Xin Liu, Hui-Jun Sun

Department of Clinical Pharmacology, College of Pharmacy, Dalian Medical University, 9 West Section, Lushan South Road, Lushunkou District, Dalian 116044, Liaoning Province, China

Correspondence: Hui-Jun Sun, e-mail: sunhujun@hotmail.com

Abstract:
The present study investigated the effect and possible mechanisms of α-lipoic acid (LA) in preventing endothelial cell injury induced by oxidized low-density lipoprotein (oxLDL). A model of human umbilical vein endothelial cell (HUVEC) injury was established by incubating the HUVECs with 200 μg/ml oxLDL. HUVECs were pre-treated with 0.1, 0.2 or 0.5 mmol/L of LA in the presence of oxLDL for 24 h. Apoptosis and cellular surface ceramide content were investigated separately by flow cytometry and by LC-MS/MS. LOX-1, Bcl-2 and CRP protein expression levels were evaluated by western blotting. LOX-1 mRNA expression was evaluated by RT-PCR assay. The results showed that oxLDL induced cytotoxicity in both concentration-dependent and time-dependent manners. LA boosted the cell survival rate and significantly reduced the content of MDA and lactate dehydrogenase (LDH) leakage. Apoptotic rates were significantly reduced by the addition of LA compared to oxLDL group. LA might also inhibit ceramide generation induced by oxLDL in a dose-dependent manner. Furthermore, LA down-regulated LOX-1 protein and mRNA expression and up-regulated Bcl-2 protein expression levels in a dose-dependent manner. Expression of CRP protein was weak and undetectable. These results suggested that LA exhibited cytoprotective effects against oxLDL by decreasing apoptotic rates and decreasing cellular surface ceramide content, two effects that are related to decreased LOX-1 expression, and also by stimulating the expression of Bcl-2 protein. The cytoprotective effects are not thought to be due to inhibited C-reactive protein (CRP) protein expression in HUVECs.

Key words:
oxidized low density lipoprotein, α-lipoic acid, HUVEC, apoptosis