Barrier protective effect of asiatic acid in TNF-α-induced activation of human aortic endothelial cells

ABSTRACT

Background: Endothelial cell activation is characterized by increased endothelial permeability and increased expression of cell adhesion molecules (CAMs). This allows monocyte adherence and migration across the endothelium to occur and thereby initiates atherogenesis process. Asiatic acid is a major triterpene isolated from Centella asiatica (L.) Urban and has been shown to possess anti-oxidant, anti-hyperlipidemia and anti-inflammatory activities. Purpose: We aimed to investigate protective effects of asiatic acid on tumor necrosis factor-Ŭ (TNF-Ŭ)-induced endothelial cell activation using human aortic endothelial cells (HAECs). Study design: For cell viability assays, HAECs were treated with asiatic acid for 24 h. For other assays, HAECs were pretreated with various doses of asiatic acid (10ï 40 µM) for 6 h followed by stimulation with TNF-Ŭ (10 ng/ml) for 6 h. Methods: Fluorescein isothiocyanate (FITC)-dextran permeability assay was performed using commercial kits. Total protein expression of CAMs such as E-selectin, ICAM-1, VCAM-1 and PECAM-1 as well as phosphorylation of IəB-Ŭ were determined using western blot. The levels of soluble form of CAMs were measured using flow cytometry. Besides, we also examined the effects of asiatic acid on U937 monocyte adhesion and monocyte migration in HAECs using fluorescent-based assays. Results: Asiatic acid significantly suppressed endothelial hyperpermeability, increased VCAM-1 expression and increased levels of soluble CAMs (sE-selectin, sICAM-1, sVCAM-1 and sPECAM-1) triggered by TNF-Ŭ. Neither TNF-Ŭ nor asiatic acid affects PECAM-1 expression. However, asiatic acid did not inhibit TNF-Ŭ-induced increased monocyte adhesion and migration. Interestingly, asiatic acid suppressed increased phosphorylation of IəB-Ŭ stimulated by TNF-Ŭ. Conclusion: These results suggest that asiatic acid protects against endothelial barrier disruption and this might be associated with the inhibition of NF-əB activation. We have demonstrated a novel protective role of asiatic acid on endothelial function. This reveals the possibility to further explore beneficial effects of asiatic acid on chronic inflammatory diseases that are initiated by endothelial cell activation.

Keyword: Asiatic acid; TNF-Ŭ; Human aortic endothelial cells; Cell adhesion molecules; NF-əB