

Asiaticoside inhibits TNF- α -induced endothelial hyperpermeability of human aortic endothelial cells

ABSTRACT

The increase in endothelial permeability often promotes edema formation in various pathological conditions. Tumor necrosis factor- α (TNF- α), a pro-atherogenic cytokine, impairs endothelial barrier function and causes endothelial dysfunction in early stage of atherosclerosis. Asiaticoside, one of the triterpenoids derived from *Centella asiatica*, is known to possess antiinflammatory activity. In order to examine the role of asiaticoside in preserving the endothelial barrier, we assessed its effects on endothelial hyperpermeability and disruption of actin filaments evoked by TNF- α in human aortic endothelial cells (HAEC). TNF- α caused an increase in endothelial permeability to fluorescein isothiocyanate (FITC)-dextran. Asiaticoside pretreatment significantly suppressed TNF- α -induced increased permeability. Asiaticoside also prevented TNF- α -induced actin redistribution by suppressing stress fiber formation. However, the increased F to G actin ratio stimulated by TNF- α was not changed by asiaticoside. Cytochalasin D, an actin depolymerizing agent, was used to correlate the anti-hyperpermeability effect of asiaticoside with actin cytoskeleton. Surprisingly, asiaticoside failed to prevent cytochalasin D-induced increased permeability. These results suggest that asiaticoside protects against the disruption of endothelial barrier and actin rearrangement triggered by TNF- α without a significant change in total actin pool. However, asiaticoside seems to work by other mechanisms to maintain the integrity of endothelial barrier rather than stabilizing the F-actin organization.

Keyword: Actin cytoskeleton; Asiaticoside; Endothelial permeability; Human aortic endothelial cell; Tumor necrosis factor- α