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ACETYLSALICYLIC ACID CONCENTRATION-DEPENDENTLY INHIBITS ENDOTHELIAL MONOCYTE ADHESION BY A MECHANISM RELATED TO ITS OXYGEN RADICAL-SCAVENGING EFFECT.

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Monocyte rolling and monocyte adhesion to endothelial cells are early steps in the initiation and progression of atherosclerosis. These pathophysiological events are related to vascular oxidative stress. Acetylsalicylic acid (ASA) has been reported to protect endothelial cells from oxidative injury, probably by an anti-oxidant mechanism. We studied the effects of ASA, salicylic acid (SA), and ibuprofen (IBU), on endothelial monocyte adhesion and formation of 8-iso-prostaglandin F2 (a marker for lipid peroxidation) in vitro. Transformed human endothelial cells (ECV304 cells) were incubated with TNFa (200 U/ml), native LDL (nLDL, 300 mg/dl), or oxidized LDL (oxLDL, 30 mg/dl) for 4 hours. After washing, human THP-1 monocytes were added and co-incubated for 30 min. After repeated washing. adhering monocytes were identified by computer-aided image analysis system. Formation of 8-iso-PGF2 was determined by gas chromatography-tandem mass spectrometry in conditioned endothelial cell media. Monocyte adhesion was significantly increased by TNF (+167±13%, $p < 0.05$) and by oxLDL (+99±12%, $p<0.05$). Native LDL (100-300 mg/dl) concentration-dependently increased monocyte adhesion (maximum at 300 mg/dl: +83±12%; $p < 0.05$). ASA significantly reduced monocyte adhesion induced by nLDL, oxLDL, or TNFo in a concentration-dependent manner. The minimum concentration of ASA which significantly reduced adhesion was 50-100 µM; almost complete inhibition was reached with 1 mM ASA. SA had a weaker inhibitory effect on monocyte adhesion, which was also significant in higher concentrations, but IBU did not significantly reduce monocyte adhesion. Addition of 300 mg/dl of NLDL to endothelial cells increased 8-iso-PGF2 release by 95±18% ($p < 0.01$). ASA (100 µM) reduced nLDL-mediated release of 8-iso-PGF2 by 77±17% ($p < 0.01$). SA also reduced lipid peroxidation (by 55±16%, $p < 0.05$), but IBU had no significant effect. We conclude that ASA exerts an anti-oxidant action on cultured human endothelial cells incubated in the presence of nLDL, and thereby reduces endothelial monocyte adhesion. SA had a similar, albeit weaker effect, whereas IBU did not inhibit 8-iso-PGF2x formation or monocyte adhesion. These findings suggest that mechanism(s) other that cyclooxygenase inhibition may underlie this phenomenon. Reduced endothelial monocyte adhesion by ASA may be a clinically important consequence of its anti-oxidant action.

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