Anandamide inhibits endothelin-1 production by human cultured endothelial cells: A new vascular action of this endocannabinoid

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The endogenous cannabinoid receptor agonist anandamide (AEA) exerts vascular effects such as vasodilatation and hypotension. In this study, we determined the effect of AEA on endothelin-1 production by cultured human umbilical vein endothelial cells. Anandamide (?5 ?mol/l) significantly decreased endothelin-1 production in a dose-dependent manner, a response not affected by the specific CB 1 receptor antagonist/inverse agonist SR-141716A. Adenosine, via activation of adenosine receptors (also targets for SR-141716A), was not involved in these effects. Conversely, AEA increased nitric oxide (NO) production, an effect inhibited by SR-141716A, indicating the involvement of CB 1 receptors. Therefore, we hypothesize that AEA effects on endothelial cells may lead to vasodilatation through independent concerted mechanisms, involving a non-CB 1 receptor-dependent inhibition of endothelin-1 production and a CB 1-mediated increase of NO.