Evodiamine inhibits in vitro angiogenesis: Implication for antitumorgenicity

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摘要

Abstract

Evodiamine, the major bioactive compound isolated from Chinese herbal drug named Wu-Chu-Yu, has been reported to exhibit anti-tumor growth and metastasis. However, the effect of evodiamine on angiogenesis remains to be investigated. We used the fresh medium containing evodiamine or human lung adenocarcinoma cell (CL1 cells) derived conditioned media free of evodiamine to test their capability to induce in vitro angiogenesis, i.e., human umbilical vein endothelial cells (HUVECs) tube formation and invasion. We demonstrated that evodiamine could directly inhibit in vitro HUVECs tube formation and invasion. Locally administered evodiamine also inhibited the in vivo angiogenesis in the chick embryo chorioallantoic membrane (CAM) assay. The gene expression of vascular endothelial growth factor (VEGF) and the p44/p42 mitogen-activated protein kinase (MAPK, ERK) that correlated with endothelial cells angiogenesis were inhibited by evodiamine. We found that the evodiamine-treated CL1 cells derived conditioned medium showed decreased VEGF release and reduced ability of inducing in vitro tube formation. After the collection of conditioned media, the VEGF expression of remaining CL1 cells were determined by Western analyses and revealed that evodiamine decreased VEGF expression. Moreover, administration of recombinant human VEGF(165) (rhVEGF(165)) induced tube formation and ERK phosphorylation by HUVECs, and partially attenuated inhibitory effect of evodiamine. From these results, we suggested that evodiamine is a potent inhibitor of angiogenesis. The mechanism might involve at least the inhibition of VEGF expression, probably through repression of ERK phosphorylation