Ethoxyfagaronine, a synthetic analogue of fagaronine that inhibits vascular endothelial growth factor-1, as a new anti-angiogeneic agent

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Résumé en anglais	Angiogenesis plays a pivotal role in tumorigenesis and also contributes to the pathogenesis of hematologic malignancies. A number of plant compounds have shown efficacy in preclinical and clinical studies and some of them possess an anti-angiogenic activity. Our present findings report anti-angiogenic activities of ethoxyfagaronine (etxfag), a synthetic derivative of fagaronine. Once determined the non-cytotoxic concentration of etxfag, we showed that the drug inhibits VEGF-induced angiogenesis in a Matrigel™ plug assay and suppresses ex vivo sprouting from VEGF-treated aortic rings. Each feature leading to neovascularization was then investigated and results demonstrate that etxfag prevents VEGF-induced migration and tube formation in human umbilical vein endothelial cells (HUVEC). Moreover, etxfag also suppresses VEGF-induced VEGFR-2 phosphorylation and inhibits FAK phosphorylation at Y-861 as well as focal adhesion complex turnover. Beside these effects, etxfag modifies MT1-MMP localization at the endothelial cell membrane. Finally, immunoprecipitation assay revealed that etxfag decreases VEGF binding to VEGFR-2. As we previously reported that etxfag is able to prevent leukemic cell invasiveness and adhesion to fibronectin, all together our data collectively support the anti-angiogenic activities of etxfag which could represent an additional approach to current anti-cancer therapies.
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