The anthraquinone derivative, DINOAQ, inhibits angiogenesis by suppressing VEGFR-mediated signaling in endothelial cells

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Vascular endothelial growth factor (VEGF) and its receptors (VEGFRs) play a critical role in regulating angiogenesis. In an effort to discover more effective inhibitors to block tumor angiogenesis, a series of anthraquinone derivatives were synthesized. Among them, 1, 8-dihydroxy-4,5-dinitroanthracene-9,10-dione(DINOAQ) was explored its anti-angiogenic mechanisms. DINOAQ significantly inhibited VEGF-induced proliferation, migration, invasion, and tube formation of HUVECs. DINOAQ also attenuated VEGF-induced microvessel sprouting from aortic rings *ex vivo* and suppressed new vasculature formation in implanted matrigel plugs in *in vivo* angiogenesis animal models. Additionally, DINOAQ inhibited VEGF-induced phosphorylation of VEGFR and its downstream protein kinases including Akt, ERK, FAK and Src. This study provides evidence that DINOAQ suppresses tumor angiogenesis through inhibiting VEGFR signaling pathways, suggesting that DINOAQ is a promising candidate for developing anti-angiogenic agent against cancer and angiogenesis-related diseases.