

Ellagic acid, a phenolic compound, exerts anti-angiogenesis effect through VEGF production and VEGFR-2 signaling pathway

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Ellagic acid (EA) is natural phenolic constituent widely found in various berries, nuts and woody plants. It was reported that EA interfered with some angiogenesis-dependent pathologies. Yet the mechanisms involved were not fully understood. Thus we analyzed its anti-angiogenic effects and mechanisms on human breast cancer utilizing *in vitro* and *in vivo* methodologies. Effects of EA on VEGF secretion were detected by Elisa and RT-PCR assay using human breast cancer cell lines MCF-7 and MDA-MB-231. The influences of EA on endothelial cells were studied by proliferation, tube formation and migration experiments. Western blotting and gelatin zymography were utilized to explore the effects of EA on VEGFR-2 induced signaling pathway. Chorioallantoic membrane model and breast cancer xenografts were built to determine the anti-angiogenic effects of EA *in vivo*. We found that EA significantly inhibited cell viability of VEGF secretion of breast cancer cell lines. The VEGF-induced angiogenic processes including proliferation, migration and tube formation of human umbilical vein endothelial cells were also suppressed. We also found that EA could directly inhibit VEGFR-2 tyrosine kinase activity and VEGFR-2/MAPK pathways in endothelial cells. EA significantly inhibited neovessel formation in chick chorioallantoic membrane and tumor growth in mouse xenografts. The microvessel density and the VEGF and P-VEGFR-2 expression in tumors treated with EA were also significantly decreased. Taken together, EA can exert anti-angiogenesis effect through both VEGF production and VEGFR-2 signaling pathway.

Biography

Wang Neng is pursuing her MPhil degree in the direction of cancer prevention in school of Chinese Medicine at University of Hong Kong. The research interests of our team can be divided into following directions: (1) Identification of cancer prevention molecular targets; (2) Isolation and determination of active components from natural plants.