

Sini Decoction containing serum modulates the expression of angiogenesis-associated molecules in HUVECs by regulating the signalling pathway VEGF-Dll4/Notch1 and p38MAPK/ERK1/2/p-AKT

Yalan Qiu^{1,2#}, Qing Song^{1#}, Yunyi Zhai¹, Lei Wang³, Binbin Cheng^{4,5*} & Jingdong Gao^{1*}

¹Department of Medical Oncology, Suzhou Traditional Chinese Medicine Hospital Affiliated to Nanjing University of Chinese Medicine, Suzhou 215009, China

²Kunshan Hospital of Traditional Chinese Medicine, Kunshan 215000, China

³Department of Hematology, Suzhou Traditional Chinese Medicine Hospital Affiliated to Nanjing University of Chinese Medicine, Suzhou 215009, China

⁴Oncology Department of Traditional Chinese Medicine, the First Affiliated Hospital of Naval Medical University, Shanghai 200433, China

⁵Faculty of Traditional Chinese Medicine, Naval Medical University, Shanghai 200043, China

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Angiogenesis is crucial for tumour growth and metastasis. Vascular endothelial growth factor (VEGF) and Notch ligand Delta-like 4 (Dll4) play a critical role in vessel formation and angiogenesis. This study aimed to determine anti-angiogenesis effects of Sini Decoction serum on human umbilical vein endothelial cells (HUVECs). We prepared Sini Decoction serum in doses of 0.925, 1.85, 3.7 g/mL, and administered to HUVECs. HUVECs migration was evaluated using a wound healing assay. Formation of tube-like structures in HUVECs was observed using a tube-formation assay. Gene transcriptions of *Dll4*, *Notch1*, *VEGF receptor 2 (VEGFR-2)* and *VEGF* were examined using a PCR assay. Protein expressions of Janus kinase-2/signal transducer and activator of transcription 3 (*JAK2/STAT3*) molecules and signal molecules downstream of *VEGF/VEGFR* related to angiogenesis (including mitogen-activated protein kinase (p38MAPK), extracellular signal-regulated kinase-1/2 (ERK1/2), focal adhesion kinase (FAK) and phosphorylated protein kinase B (p-Akt)) were detected by western blot. Sini Decoction serum significantly inhibited cell migration and the formation of tube-shaped structures in HUVECs compared to Control group ($P < 0.05$). Sini Decoction serum markedly decreased *Dll4*, *Notch1*, *VEGF*, and increased *VEGFR-2* gene transcriptions, compared to those of Control group ($P < 0.05$). Sini Decoction serum significantly reduced expression of p-Akt, p38MAPK and ERK1/2, compared to Control group ($P < 0.05$). Although a reduction in FAK and STAT3 expression was discovered in HUVECs administered by Sini Decoction serum, without statistical significance compared to Control group ($P > 0.05$). In conclusion, Sini Decoction serum modulated the expression of angiogenesis-associated molecules in HUVECs by activating VEGF-Dll4/Notch1 and p38MAPK/ERK1/2/p-AKT signalling pathways.

Keywords: Traditional Chinese Medicine, Medical oncology, Treatment, Vascular endothelial cells