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Abstract

The Proangiogenic Effect of Saponins from *Panax Notoginseng* in Human Umbilical Vein Endothelial Cells (HUVEC)

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Angiogenesis plays an important pathological role in a wide range of diseases, such as cancer (Folkman J, et al., 1999; Amano.M et al., 2007), various ischemic and inflammatory diseases. (Carmeliet P, et al., 2000; József TÍMÁR et al., 2001). Substantial studies have showed that researches on angiogenic effects of Chinese medicine leads to discovery of many active pro-angiogenic and anti-angiogenic compounds and novel mechanism of angiogensis (Fan T.P, et al., 2006). *Panax notoginseng*, as a commonly used "blood circulation promoting" herb in traditional Chinese medicine, is a potential candidate for the purpose.

However, certain diseases can be exacerbated by the loss of balance in angiogenesis, which results in either excessive or insufficient blood vessel formation. Diseases such as cancer, diabetic retinopathy and rheumatoid arthritis are characterized by excessive blood vessel formation while peripheral and coronary ischemia and infarction, chronic wound healing failure and ulcers are characterized by insufficient blood vessel formation.

Panax notoginseng, commonly used in the prescriptions of traditional Chinese medicine for blood circulation promotion and to be a potential candidate for the disease cure. However, the biological effects of saponin extract from *Panax notoginseng* (PNS) on angiogenesis and the underlying mechanisms are yet to be fully elucidated. This investigation describes the

angiogenic effects of PNS, ginsenoside Rg1, ginsenoside Re and notoginsenoside R1 on HUVEC *in vitro*. The extract and three monomers were identified to stimulate the proliferation of HUVEC by XTT assay and microscopic cell counting. A significant increase in numbers of invaded cells was observed in PNS and the monomers treated HUVEC using the invasion assay. In addition, we observed a significant increase in number of branch points during endothelial cell capillary formation after treatments with either PNS or the monomer. Moreover, PNS was found to enhance VEGF, KDR/Flk-1 and Flt-1 mRNA expression by real-time PCR and the PNS induced-HUVEC proliferation could be abolished by a KDR/Flk-1 inhibitor. Furthermore, the proliferations of HUVEC induced by PNS and the monomers were significantly abrogated by inhibitors of PI3K, Akt and eNOS. All results suggest that saponin extract (PNS) and its' constituents (Rg1, Re and R1) isolated from *Panax notoginseng* can promote angiogenesis in multiple models, and the pro-angiogenic effects involve VEGF- KDR/Flk-1 and PI3K-Akt-eNOS dependent signaling pathways.