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Abstract

THE PROANGIOGENIC EFFECT OF *RADIX ASTRAGALI* EXTRACT IN HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS (HUVEC)

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Angiogenesis, the formation of new blood vessels, is essential for normal growth and homeostasis in human body. 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. *Radix Astragali*, named huangqi in Chinese, is commonly used in the prescriptions of traditional Chinese medicine. In traditional systems, it is used to replenish the vital energy for the treatment of lacking strength, anorexia and loose stools, prolapse of uterus and anus, spontaneous sweating, and chronic nephritis with edema and proteinuria, and to dispel pus and accelerate the healing of chronic ulcers. The saponin astragaloside IV (AS-IV; Fig. 1), a 3-O-β-Dxylopyranosyl-6-O-β-D-glucopyranosylcycloastragenol was purified from the Chinese medical herb *Astragalus membranaceus* (Fisch) Bge, is regarded as a characteristic and active constituent of *Radix Astragali* and the content of astragaloside IV is the main criterion of its quality assurance and control..

Recently, *Radix Astragali and* astragaloside IV were proved to be a potential candidate to cure the diseases, driven by imbalanced angiogenesis. However, the biological effects of

Radix Astragali and astragaloside IV on angiogenesis and the underlying mechanisms are unclear yet. This investigation describes the angiogenic effects of *Radix Astragali* extract and astragaloside IV on HUVEC *in vitro*. The extract and its' constituent marker was identified to stimulate the proliferation of HUVEC by XTT assay and microscopic cell counting. The wound healing migration assay illustrated that the dramatic increment of migration could be measured in *Radix Astragali* extract and astragaloside IV treated HUVEC. Meanwhile, the numbers of invaded cells and the number of branching points were significantly increased in both treatment groups. In addition, Radix Astragali extract and astragaloside IV was found to enhance VEGF mRNA expression by real-time PCR, and a VEGF receptor specific blocker, SU5416, could inhibit *Radix Astragali* extract- and astragaloside IV -induced HUVEC proliferation. Furthermore, the stimulation of HUVEC cell proliferation by 12.5 μg/ml *Radix Astragali* extract and 100 μg/ml astragaloside IV could be blocked by the phosphatidylinositol 3-kinase (PI3K), Akt and endothelial nitric oxide synthase (eNOS) inhibitor (wortmannin, SH-6, L-NAME) respectively. All results suggest that *Radix Astragali* extract and astragaloside IV can promote angiogenesis in multiple models and probably through VEGF-VEGF tyrosine kinase receptor and PI3K-Akt-eNOS,