

DOCTORAL THESIS

Effects of salvianolic acid B against apoptosis and adhesion molecules expression in the vascular endothelial cells

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**Effects of Salvianolic acid B Against Apoptosis
and Adhesion Molecules Expression in the
Vascular Endothelial Cells**

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**A thesis submitted in partial fulfillment of the requirements
for the degree of
Doctor of Philosophy**

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ABSTRACT

Salvianolic acid B (Sal B) is one of the most bioactive components of *Salvia miltiorrhiza* Bge., a Chinese herbal medicine that has been commonly used for centuries to prevent and treat cerebrovascular and cardiovascular diseases. Atherosclerosis, which may occur in cerebrovascular and cardiovascular disease, is a multi-factorial disease with a strong heritable component. Apoptosis and inflammatory events in endothelial cells (ECs) contribute to the early stages of atherosclerosis. H₂O₂ and TNF- α can lead to endothelial dysfunction, reducing ECs capacity to maintain homeostasis and leading to vascular disorder. Since drugs entering into the circulation and vascular systems are exposed to blood flow-induced shear stress, it will be of interest and biologically important to investigate the effect of Sal B under laminar shear stress (LSS) condition.

The present study aimed to: (1) investigate the preventive effect of Sal B on H₂O₂-induced apoptosis in ECs, and explore the corresponding signaling transduction pathway; (2) determine the effect of LSS on the TNF- α -induced adhesion molecules expression i.e. VCAM-1, ICAM-1 and E-selectin in ECs; (3) study the combination effect of Sal B and LSS on modulating the TNF- α -induced expression of adhesion molecules in ECs. DAPI staining and TUNEL assay were used to detect the effect of Sal B on H₂O₂-induced apoptosis in ECs. LSS was applied to investigate the combined effect of Sal B and LSS on TNF- α -induced adhesion molecules expression

in ECs. The protein expression was determined by Western blot. The major findings of this study are: (1) H₂O₂ induces ECs apoptosis mainly through the PI3K/ERK pathway; (2) Sal B prevents H₂O₂-induced apoptosis predominantly through the PI3K/Akt/Raf/MEK/ERK pathway; (3) Sal B has combined inhibitory effect with LSS on TNF- α -induced adhesion molecules expression by inhibiting NF- κ B activation evidenced by I κ B α degradation and p65 nuclear translocation in ECs.

In conclusion, Sal B exerts anti-apoptosis and anti-adhesion molecule expression in vascular ECs via different signaling transduction pathways. Furthermore, Sal B and LSS work a combined inhibitory effect on TNF- α -induced expression of adhesion molecules i.e., VCAM-1, ICAM-1 and E-selectin in ECs via modulation of NF- κ B. It is believed that data from this study support the clinical application of Sal B in prevention and treatment of cardiovascular and cerebrovascular diseases.

Keywords: Salvianolic acid B; hydrogen peroxide, tumor necrosis factor α , apoptosis, PI3K, Akt, laminar shear stress; atherosclerosis; VCAM-1; ICAM-1; E-selectin; NF- κ B, I κ B α

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