

• 研究论文摘要 •

[文章编号] 1007-3949 (2011) 19-03-0274-01

## Tanshinone II-A Attenuates and Stabilizes Atherosclerotic Plaques in Apolipoprotein E Knockout Mice Fed with High Cholesterol Diet

Suowen Xu<sup>1</sup>, Yan Huang<sup>1</sup>, Peter J. Little<sup>2</sup>, and Peiqing Liu<sup>1</sup>

(1. Department of Pharmacology and Toxicology, School of Pharmaceutical Sciences, Sun Yat-sen University, Guangzhou, Guangdong 510006, China; 2. Discipline of Pharmacy, School of Medical Sciences and Diabetes Complications Group, Health Innovations Research Institute, RMIT University, Melbourne, Victoria, 3083, Australia)

**[KEY WORDS]** ApoE<sup>-/-</sup> mice; Atherosclerosis; NF- $\kappa$ B; Plaque Composition; Reactive Oxygen Species; Tanshinone

**Objective** Tanshinone II-A (Tan), a bioactive diterpene isolated from *Salvia miltiorrhiza* Bunge (Danshen), possesses anti-oxidant and anti-inflammatory activities. The present study investigated whether Tan can reduce and stabilize atherosclerotic plaques in Apolipoprotein E knockout (ApoE<sup>-/-</sup>) mice maintained on a high cholesterol diet (HCD). **Methods and Results** Six week-old mice challenged with HCD were randomly assigned to 4 groups: C57BL/6J, ApoE<sup>-/-</sup>, ApoE<sup>-/-</sup> + 30 mg/kg • d Tan and ApoE<sup>-/-</sup> + 10 mg/kg • d Tan. After 16 weeks of intervention, Tan treated mice showed decreased atherosclerotic lesion size in the aortic sinus and face aorta. Furthermore, immunohistochemical analysis revealed that Tan rendered the lesion composition a more stable phenotype as evidenced by reduced necrotic cores, decreased macrophage infiltration, increased smooth muscle cell and collagen content. Tan also significantly reduced in situ superoxide anion production, aortic expression of NF- $\kappa$ B, and matrix metalloproteinase-9 (MMP-9). In vitro treatment of RAW264.7 macrophages with Tan significantly suppressed oxidized LDL-induced reactive oxygen species production, pro-inflammatory cytokine (IL-6, TNF- $\alpha$ , MCP-1) expression, and MMP-9 activity.

**Conclusions** Tan attenuates the development of atherosclerotic lesions and promotes plaque stability in ApoE<sup>-/-</sup> mice by reducing vascular oxidative stress and inflammatory responses. Our findings highlight Tan as a potential therapeutic agent to prevent atherosclerotic cardiovascular diseases.

**[基金项目]** 国家自然科学基金(30472022); 国家科技部新药创制重大专项资助项目(2009ZX09102-452, 2009ZX09303-007); 2010 年教育部“博士研究生学术新人奖”资助

**[作者简介]** 徐素文, 博士研究生, 主要从事动脉粥样硬化、心肌肥厚发病机制研究与新药研发。通讯作者 Peiqing Liu, 博士。  
(此文编辑 文玉珊)