dl-PHPB were investigated and compared with ticlopidine. Four platelet aggregation inducers, ADP, arachidonic acid, collagen and thrombin were used in the study. It was found that puerarin and dl-PHPB specifically inhibited ADP induced platelet aggregation like ticlopidine did. However, salvianolic acid B inhibited both ADP and collagen induced platelet aggregations with similar potency. Due to existing two ADP receptor subtypes on platelets, $P2Y_1$ and $P2Y_{12}$, we studied the action of above compounds on the receptors and the signaling pathways. It was found that dl-PHPB decreased IP_1 accumulation produced by ADP, but had no effect on IP_1 level induced by m-3M3FBS, an activator of PLC. M-3M3FBS might attenuate the inhibitory effect of dl-PHPB on ADP-induced platelet aggregation. In addition, dl-PHPB did not affect cyclic AMP formation in platelets by ADP, which is different from $P2Y_{12}$ antagonist ticlopidine. Puerarin showed the similar effects of dl-PHPB. Therefore, the actions of dl-PHPB and puerarin might be through $P2Y_1$ receptor-PLC-β pathway. Salvianolic acid B did not reduce the IP_1 accumulation stimulated by ADP. It might act on the receptor subtype $P2Y_{12}$. Our results suggest that components of Chinese herb medicine might be a resource for development of novel anti-platelet drugs.

Key words: platelet aggregation; ADP receptors; Houxue Huayu

Sesamol inhibits atherogenic LDL-induced endothelial cell senescence *in vivo* and *in vitro*

Hong-kai HUANG[1*], Fang-yu CHEN[2*], Kuan-hsiang TING[3*], Chih-chung FENG[2], Chia-ming CHANG[2], Chu-huang CHEN[4,5], Ming-yi SHEN[2]

(*1. Department of Internal Medicine, Changhua Christian Hospital, Changhua, Chinese Taipei; 2. Graduate Institute of Clinical Medical Science, China Medical University, Taichung, Chinese Taipei; 3. Department of Biological Science and Technology, College of Life Sciences, China Medical University, Taichung, Chinese Taipei; 4. Section of Atherosclerosis and Lipoprotein Research, Department of Medicine, Baylor College of Medicine, Houston, Texas 77030, USA; 5. Vascular and Medicinal Research, Texas Heart Institute, Houston, Texas, USA*)

Abstract: **OBJECTIVE** Highly electronegative L5 low-density lipoprotein (LDL), an atherogenic LDL, induces endothelial cell (EC) senescence and has been implicated in the progression of atherosclerosis. We examine whether sesamol, a natural organic compound and component of sesame oil, prevents EC senescence induced by electronegative LDL (L5) and to investigate the underlying mechanisms. **METHODS** Syrian hamsters, which have a LDL profile similar to that of humans, were fed a normal chow diet (control), a high-fat diet (HFD), or a HFD supplemented with the administration of 50 or 100 $mg \cdot kg^{-1}$ sesamol via oral gavage (HFD+sesamol) for 16 weeks ($n=10$ per group). Among these groups, we compared plasma L5 levels and aortic endothelial senescence in the aortic arch. *In vitro*, we examined the effects of sesamol on human aortic endothelial cell (HAEC) senescence and signaling pathways induced by L5. **RESULTS** Hamsters in the HFD group had higher plasma L5 levels than did the HFD+sesamol groups or control group. Beta-galactosidase (gal) staining showed that aortic endothelial senescence was markedly increased in the aortic arch of the HFD group but not in that of the HFD+sesamol groups when compared with the control group. *In vitro*, treatment of HAECs with sesamol ($1-3\ mol \cdot L^{-1}$) blocked L5-induced EC senescence in a dose-dependent manner. Sesamol also markedly inhibited the L5-induced phosphorylation of p38 MAPK and p53 activation and increased Mdm2 and phosphorylation of Akt. **CONCLUSION** The critical findings of this study suggest that sesamol may provide protection against atherosclerosis and the development of cardiovascular disease in humans.

Key words: sesamol; atherogenic LDL; endothelial cell; Syrian hamsters; p53

Foundation item: The project supported by the National Science Council of Cinese Taipei (NSC102-2320-B-039-058) and China Medical University, Chinese Taipei (CMU102-N-02 and CMU103-N-08)

Corresponding author: Ming-yi SHEN, E-mail: shenmy1124@gmail.com, Tel: (+886)422052121 ext 7502

* Co-first authors.