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Abstract

ANTI-INFLAMMATORY EFFECTS OF RESVERATROL AND ITS ANALOGUES IN TNF- α -INDUCED HUMAN UMBILICAL VEIN ENDOTHELIAL CELLS (HUVEC)

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Atherosclerosis, the main cause of morbidity and mortality in developed countries, is now considered as a chronic inflammatory vascular disease. Many pathophysiologic studies have shown that the first step in its development and the most important events in inflammation is adhesion of monocytes to the vascular endothelium and their subsequent migration into the vessel wall. The activation of endothelial cells and resulting expression of adhesion molecules at sites of inflammation are of particular significance. Thus, the molecules that block these interactions have been targeted as potential therapeutic treatments for acute and chronic inflammatory diseases.

Stilbene compounds are present naturally in many plants, whose extensive biological activities have been identified. In recent years, the biological activities of stilbene compounds have been reported, including antioxidation, antitumor and anti-thrombotic action. Resveratrol (trans-3,5,4'-trihydroxystilbene), one of the most important and common stilbene compounds from *Polygonum cuspidatum*, as an important polyphenolic phytoalexin, exhibits beneficial effects to health, such as anti-cancer, cardioprotection, neuroprotection, anti-aging and anti-inflammation as shown in previous studies. And a large body of evidences point to a prominent role of resveratrol as an anti-atherosclerotic agent. Previous studies showed that resveratrol

analogues could have the similar but also differential and even opposing biological activities. Thus, this study is to investigate whether resveratrol analogues such as trans-3, 5, 4'-trimethoxystilbene (TMS) and polydatin have anti-inflammatory vascular effect and elucidate the mechanism of this effect in atherosclerosis, further in comparison with each other, we determined the effect of pharmacological doses of them upon the adhesion of THP-1 cells to human umbilical vein endothelial cells (HUVEC), as well as the expression of adhesion molecules, the translocation of NF- κ B in HUVEC. Adhesion of THP-1 cells to HUVEC was evaluated by co-culture experiments using calcein-AM-labeled THP-1 cells. The expression of adhesion molecules was evaluated by ELISA, real time-PCR and Western blot; the translocation of NF- κ B were determined by immunochemical staining assay. TNF- α was used to induce inflammatory responses in HUVEC. Our results showed that these three structurally related stilbenes also show anti-inflammatory vascular activity but with different potency. TMS appears to be more potent than RSV for treating vascular inflammation, while PD is significantly less active than both of them. The mechanism of these anti-inflammatory effects may be mainly attributed to the inhibition of NF- κ B pathway activation. These results implied that all the three investigated stilbene compounds, especially TMS exhibited potent inhibitory effect on inflammation induced cell-cell adhesion and expression of adhesion molecules, and activation of NF- κ B pathway. Therefore, it could be potentially developed as an alternative in the prevention and treatment of chronic inflammatory diseases such as atherosclerosis.

Keywords : stilbene; inflammation; resveratrol; atherosclerosis; cell adhesion molecules; NF- κ B pathway