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Cytoprotective effects of CSTMP, a novel stilbene derivative, against H_2O_2-induced oxidative stress in human endothelial cells

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Abstract:
A novel stilbene derivative, (E)-2-(2-chlorostyryl)-3,5,6-trimethylpyrazine (CSTMP), was designed and synthesized based on the pharmacophores of tetramethylpyrazine (TMP) and resveratrol (RES). In the present study, we investigated the protective effects of CSTMP on vascular endothelial cells under oxidative stress and elucidated its molecular mechanisms. The radical scavenging activity of CSTMP was assessed by the DPPH test. Human Umbilical Vein Endothelial Cells (HUVECs) were exposed to 150 μM hydrogen peroxide (H_2O_2) for 12 h, resulting in a decrease of cell viability assessed by the MTT assay and an increase of apoptotic cells assessed by the nuclear staining assay and flow cytometry. The activities of lactate dehydrogenase (LDH), superoxide dismutase (SOD) and nitric oxide synthase (NOS) and the contents of malondialdehyde (MDA), reduced glutathione (GSH) and nitric oxide (NO) in cells were determined by commercial kits. The expression levels of pro-apoptotic factor caspase-3 and anti-apoptotic signal ERK1/2 were detected by western blot. The results showed that CSTMP had a moderate anti-oxidative effect against the DPPH test, which was less than RES. Co-incubation with CSTMP increased the cell viability, markedly reduced the LDH leakage from the cells and decreased the lipid peroxidation. These effects of CSTMP were accompanied by increasing activity of the endogenous antioxidant enzyme SOD, the level of GSH, the production of NO and cNOS activity. Moreover, CSTMP showed stronger effects on the inhibition of apoptosis, caspase-3 expression, and the activation of phosphorylated ERK1/2 compared to RES. Furthermore, CSTMP could inhibit the expression of phospho-JNK and phospho-p38 induced by H_2O_2. These results suggest that CSTMP prevents H_2O_2-induced cell injury through anti-oxidation and anti-apoptosis *via* the MAPK and caspase-3 pathways.

Key words:
(E)-2-(2-chlorostyryl)-3,5,6-trimethylpyrazine, oxidative stress, apoptosis, antioxidation, NO, MAPK, caspase-3