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INHIBITORY EFFECT OF REINIOSIDE C ON VASCULAR SMOOTH MUSCLE CELLS PROLIFERATION INDUCED BY ANGIOTENSIN II VIA INHIBITING NADPH OXIDASE-ROS-ERK1/2-NF-KB-AP-1 PATHWAY

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Objectives Proliferation of vascular smooth muscle cells (VSMCs) induced by angiotensin II (Ang II) plays a vital role in the pathogenesis of hypertension. In the present study, the effect of reinioside C, a main active ingredient of Polygalafallax Hemsl, on proliferation of VSMCs induced by Ang II was investigated.

Methods Cell proliferation was measured by two methods; the DNA synthesis and cell cycle were analysed by BrdU marking and flow cytometry. Intracellular ROS level were determined by measuring the oxidative conversion of cell permeable H2DCF to DCF in fluorospectrophotometer. NADPH oxidase subunits (p22phox, gp91phox), AP-1 subunits (c-fos, c-jun) and c-myc were evaluated by real time PCR. ERK1/2 and IkB-a were measured by western-blot. The electrophoretic mobility shift assay for determining the NF-kB DNA-binding activity.

Results The results showed that reinioside C attenuated Ang II-induced NADPH oxidase mRNA expression, generation of ROS, ERK1/2 phosphorylation and activation of NF-kB as well as mRNA expression of AP-1 and c-myc in VSMCs in a concentration-dependent manner. These effects of Ang II were also inhibited by diphenyleneiodonium (the NADPHoxidase inhibitor), PD98059 (the ERK1/2 inhibitor) and pyrollidinedithiocarbamate (the NF-kB inhibitor).

Conclusions These result suggest reinoside C attenuates AngII-induced proliferation of VSMC via inhibiting NADPH oxidase- ROS- ERK1/2-NF-kB -AP-1 pathway.