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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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¹Dan Hong, ¹Rui-Zheng Shi, ¹Yong-Ping Bai, ²Chang-Ping Hu, ³Gui-Shan Tan, ²Yuan-Jian Li, ¹Tian-Lun Yang, ³Kang-Ping Xu, ¹Guo-Gang Zhang. ¹*Department of Cardiovascular Medicine, Xiangya Hospital, Central South University;* ²*Department of Pharmacology, School of Pharmaceutical Sciences, Central South University;* ³*Department of Medicinal Chemistry, School of Pharmaceutical Sciences, Central South University*

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 reinoside 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 I κ B- α were measured by western-blot. The electrophoretic mobility shift assay for determining the NF- κ B DNA-binding activity.

Results The results showed that reinoside C attenuated Ang II-induced NADPH oxidase mRNA expression, generation of ROS, ERK1/2 phosphorylation and activation of NF- κ B 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 pyrrolidinedithiocarbamate (the NF- κ B inhibitor).

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