Dung-shen (*Codonopsis pilosula*) attenuated the Cardiac-impaired Insulin-like Growth Factor II Receptor Pathway on Myocardial Cells

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Abstract

Previous studies from our lab showed that increase in AngII in H9c2 cells causes elevated IGFII and IGFIIR through MEK and JNK, leading to rise in intracellular calcium, calcineurin activation by PLC-β3 *via* Gαq, insertion into mitochondrial membranes of Bad, and apoptosis *via* caspases 9 and 3. *Codonopsis pilosula* is traditionally used to lower blood pressure. The purpose of our study is to investigate if *C. pilosula* attenuates AngII plus Leu^{27}-IGFII-induced calcium influx and apoptosis in H9c2 cardiomyoblasts. *C. pilosula* significantly attenuated AngII induced IGFIIR promoter activity. Leu^{27}-IGFII was applied to enhance the AngII effect. *C. pilosula* also reversed Ca^{2+} influx, MOMP and apoptosis increased by AngII plus Leu^{27}-IGFII. Molecular markers in IGFIIR apoptotic pathway (IGFIIR, calcineurin, etc.) and IGFIIR-Gαq association were downregulated by *C. pilosula*. However, p-Bad^{Ser136}

and Bcl-2 were increased. Therefore, *C. pilosula* suppresses AngII plus Leu^{27}-IGFII-induced IGFII/IGFIIR pathway in myocardial cells.

Key words: angiotensin II, apoptosis, calcium influx, *Codonopsis pilosula*, leucine^{27}-insulin like growth factor II, mitochondrial outer-membrane permeability