Young Investigator Award

Compound A, a Ginger Extract, Significantly Reduces Pressure Overload-induced Systolic Heart Failure in Mice

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Citation: *European Cardiology Review* 2021;16:e57. **DOI:** https://doi.org/10.15420/ecr.2021.16.PO1

Objectives: Cardiac remodelling is a compensatory mechanism associated with cardiomyocyte hypertrophy and cardiac fibrosis. This process eventually results in chronic heart failure. In this study, we screened a natural compound library for compounds that suppress both hypertrophic and fibrotic responses, and found compound A, a ginger extract. The purpose of this study is to investigate the effect of compound A on cardiomyocyte hypertrophy, cardiac fibrosis and the development of heart failure.

Materials and methods: First, primary cultured cardiomyocytes and cardiac fibroblasts were treated with 1 μM compound A, then stimulated with phenylephrine or transforming growth factor-β (TGF-β), respectively. Immunofluorestaining and qPCR were performed on cardiomyocytes. Measurement of L-proline incorporation, qPCR and western blotting were carried out on cardiac fibroblasts. C57BL/6J mice were subjected to transverse aortic constriction (TAC) surgery, then given a daily oral administration of 1 mg/kg compound A for 8 weeks. Echocardiographic analysis and measurement of heart weight to body weight (HW/BW) ratio were performed.

Results: In cultured cardiomyocytes, 1 μM of compound A suppressed phenylephrine-induced increases in the surface area of cardiomyocytes and in the mRNA levels of ANF and BNP. In cultured cardiac fibroblasts, the compound also suppressed TGF-β-induced L-proline incorporation, and mRNA and protein levels of α-smooth muscle actin. In heart failure model mice, echocardiographic analysis showed that 1 mg/kg of compound A prevented a TAC-induced increase in posterior wall thickness and a decrease in systolic dysfunction. The compound also suppressed a TAC-induced increases in HW/BW ratio.

Conclusion: Compound A may be an effective agent for heart failure therapy. ❑