Chrysanthemum morifolium Extract Prevents the Development of Doxorubicin-induced Heart Failure

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Objectives: Doxorubicin, an anthracycline anticancer drug, induces a cumulative and dose-dependent cardiotoxicity. Recently, *Chrysanthemum morifolium* extract (CME), produced from the purple chrysanthemum flower, has been reported to possess various physiological activities, such as antioxidant and anti-inflammatory effects. However, it is unknown whether CME prevents doxorubicin-induced cardiotoxicity. The aim of this study is to investigate the effectiveness of CME against doxorubicin-induced cardiotoxicity.

Materials and methods: H9C2 cardiomyocytes were treated with CME for 2 hours, and then stimulated with 1 µM doxorubicin. After 24 hours incubation, surviving cells were evaluated by MTT assay. Cellular apoptosis markers were assessed by western blotting. Next, to investigate the effect of CME on doxorubicin-induced cardiomyopathy *in vivo*, C57BL6 mice were orally administered with CME (400 mg/kg/day) or vehicle daily for 2 days before being treated with doxorubicin (20 mg/kg) intraperitoneally once. At 7 days after doxorubicin injection, an echocardiographic analysis and a TUNEL assay were performed.

Results: Administering 1 mg/ml CME significantly reduced doxorubicin-induced cytotoxicity in H9C2 cells. Western blotting showed that CME suppressed doxorubicin-induced increases in four markers of apoptosis: p53, phosphorylated p53, and cleaved caspase-9 and -3. The survival ratio of the CME-treated group was significantly higher than that of the vehicle-treated group *in vivo*. CME significantly improved doxorubicin-induced left ventricular systolic dysfunction and suppressed doxorubicin-induced apoptosis in mice.

Conclusion: This study indicates that CME treatment reduces doxorubicin-induced cardiotoxicity by suppressing apoptosis. Further studies are expected to apply CME in clinical settings for the prevention of doxorubicin-induced heart failure. ❑