

Cardioprotective effects of silymarin in heart failure for adjunctive therapy: Role of Nrf2 signal transduction pathway

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In the present study, the potential of silymarin (SIL) administration as an adjuvant therapy in heart failure (HF) model of rats was investigated. HF induction was done by injecting 85 mg/kg/day isoproterenol and silymarin (SIL), trimetazidine (TMZ) and SIL+TMZ were administered to HF rats for 2 weeks. Then, echocardiography parameters such as ejection fraction (EF) and fractional shortening (FS) were evaluated. The anxiety and depression like behaviours were evaluated by elevated plus maze (EPM) and sucrose preference test (SPT). Furthermore, the plasma levels of BNP, Galectin-3 and Nrf2, as well as the serum levels of cytokines IL-1 β , IL-6 and TNF- α were measured. Finally, the expression levels of *SOD1*, *Gpx1* and *NQO1* genes were measured using RT-PCR technique. Administration of SIL, TMZ and SIL+TMZ to HF rats for 2 weeks was associated with improvement of EF and FS parameters. Also, all treatments improved animals function in both EPM and SPT tests. Furthermore, decreases in the plasma levels of BNP and Galectin-3 and an up-regulation of Nrf2 were observed in HF rats receiving SIL, TMZ and SIL+TMZ. In addition, downregulation of IL-1 β , IL-6 and TNF- α cytokines and overexpression of *SOD1*, *Gpx1* and *NQO1* genes were seen in HF rats after administration of SIL, TMZ and SIL+TMZ. Silymarin has the potential to be used as an adjunctive therapy in heart failure.

Keywords: Gene, Parameter, Cytokine, Galectin-3, B-type natriuretic peptide