

Pristimerin Protects Against Doxorubicin-Induced Cardiomyopathy and Fibrosis

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BACKGROUND

Pristimerin (Pris) is triterpenoid compound with many biological effects. Until now, nothing is known about its effect on doxorubicin (DOX)-induced cardiotoxicity. Hence, this study investigated the impact of Pris on DOX-induced cardiotoxic effects.

MATERIALS AND METHODS

Rats were treated with Pris 1 week before and 2 weeks contaminant with repeated DOX injection. Afterwards, electrocardiography (ECG), biochemical, histopathological, PCR, and Western blot assessments were performed.

RESULTS

Pris effectively alleviated DOX-induced deleterious cardiac damage. It inhibited DOX induced ECG abnormalities as well as DOX-induced elevation of serum indices of cardiotoxicity. The histopathological cardiac lesions and fibrosis were remarkably improved in Pris-treated animals. Pris reduced hydroxyproline content and attenuated the mRNA and protein expression of the pro-fibrogenic genes. The antioxidant

activity of Pris was prominent through the amelioration of oxidative stress parameters and enhancement of antioxidants. Furthermore, Pris enhanced the activation of nuclear factor-erythroid 2 related factor 2 (Nrf2) signaling pathway as it increased the mRNA and protein expression of Nrf2 and Nrf2-dependent antioxidant genes (GCL, NQO1, HO-1). Additionally, the anti-inflammatory effect of Pris was obvious through the inhibition of mitogen activated protein kinase (MAPK)/nuclear factor kappa-B (NF-kB) signaling and subsequent inhibition of inflammatory mediators.

CONCLUSION

This study provides evidence of the cardioprotective activity of Pris which is related to the modulation of Nrf2 and MAPK/NF-kB signaling pathways.

KEYWORDS

doxorubicin, pristimerin, cardiotoxicity, Nrf2, MAPK/NF-kB