

ABSTRACT

Drug induced liver injury (DILI) is an important detrimental event manifesting as a spectrum from mild liver enzyme elevation to fibrosis, cirrhosis and even liver failure. It is one of the main causes of drug withdrawal during pre-clinical and clinical phases. At present, DILI treatment is restricted to glucocorticoids, immunosuppressant, anticoagulants and, ursodeoxycholic acid (UDCA). Therefore, there is a requirement of other therapeutic alternatives for managing DILI. The objective of this study was to evaluate the ameliorative effect of nicorandil on hepatic damage induced by alpha-naphthyl isothiocyanate (ANIT). Thirty two male albino mice were randomly divided into four groups; control, ANIT, nicorandil and milk thistle group. Control group received standard diet and water along with 0.5% CMC (via oral gavage). ANIT group received 0.5% CMC daily and an oral dose of ANIT (75mg/kg) dissolved in olive oil once on 7th day after the last dosage of CMC with a gap of 1 hour. Nicorandil group was administered nicorandil (100mg/kg) suspended in 0.5% CMC orally for 7 days and a single dose of ANIT (75mg/kg) on 7th day. Milk Thistle group serving as a comparison group was given milk thistle (600mg/kg) for 7 days and single dose of ANIT (75mg/kg) on 7th day. After 48 hours of ANIT administration mice were euthanized to collect blood serum (for liver function test) and liver tissue (for histopathological examination). The result showed a notable elevation in serum levels of ALT, ALP, AST and total bilirubin of ANIT group as compared to control group which indicated an injured liver. The liver enzymes and bilirubin level was significantly lesser in Nicorandil group as compared to ANIT group. The values of liver parameters of Nicorandil xvii

group were comparable to control group and milk thistle group, indicating hepatoprotective effect of nicorandil. Furthermore, histopathological examination indicated that the liver of ANIT group was damage whereas liver cells in Nicorandil group remained intact. In conclusion, our results showed ameliorative outcome of nicorandil against ANIT induced liver damage.

Keywords: Nicorandil, ANIT, DILI