

Adriamycin induced cardiotoxicity and the possible protective role of Silymarin in adult male albino rat : A light and electron microscopic study .

Thesis

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SUMMARY

Adriamycin is one of the most effective and useful antineoplastic agents for the treatment of a variety of malignancies , including lymphoma , leukemia and solid tumors . However , its therapeutic use is sometimes limited by late onset acute and chronic cardiotoxicity . The chronic cardiotoxicity is dose dependent and causes irreversible myocardial damage , resulting in dilated cardiomyopathy with fatal congestive heart failure .

Previous studies reported that free radicals – mediated myocyte damage , disturbance in myocardial adrenergic function , intracellular calcium overload and release of cardiotoxic cytokines e.g tumor necrosis factor , might be involved in the pathogenesis of adriamycin induced cardiomyopathy .

Silymarin , an antioxidant flavenoid complex derived from the herb milk thistle (*Silybum marianum*) , has long been used in treatment of liver diseases , these properties seems to be due to their ability to scavenge free radicals and to chelate metal ions . Recently , silymarin received attention due to its alternative beneficial activities as hypocholesterolemic and cardioprotective agent . It could be very effective in the cardioprotective application during cancer treatment with cardiotoxic drugs as adriamycin .

In the current study forty adult male albino rats weighting (200-250) gms were used . they were divided into 4 groups(10 rats in each group) as follows :

Group I (control group) :

The rats were intraperitoneally injected with saline daily for 10 days .

Group II (Adriamycin group) :

The rats were intraperitoneally injected with a single dose of adriamycin (10 mg / kg) on the seventh day of the experiment , which induces cardiotoxicity in rats .

Group III (Silymarin group) :

The rats were intra peritoneally injected with silymarin dissolved in saline in a dose of (50 mg /kg) daily for 10 days .

Group IV (Adriamycin + Silymarin group) :

The rats were injected intra peritoneally with silymarin in a dose of (50 mg /kg) daily for seven days before adriamycin and daily thereafter for 72 hours .

All rats were sacrificed after 72 hous of adriamycin injection by high dose ether and prepared for :

(A) Biochemical study :

Blood samples were collected from all groups after 72 hours of adriamycin injection and the following were estimated :

Cardiac enzymes (LDH , CPK) , serum cholesterol and total lipids .

Injection of the rats with a single dose of adriamycin (10mg/kg) caused a significant increase in both plasma CPK and LDH enzyme activities compared to their control values . After 72 hours of adriamycin injection , the level of this increase was 10 and 2.5 folds their control values respectively . Pre treatment of adriamycin injected rats with silymarin (50mg/kg) 7 days before adriamycin and daily thereafter for 72 hours resulted in a significant decrease in plasma CPK and LDH levels compared to their respective adriamycin injected rats .

Also injection of rats with a single dose of adriamycin (10mg/kg) caused a significant increase in both plasma cholesterol and triglycerides compared to their control values . Pre treatment of adriamycin injected rats with silymarin (50mg/kg) 7 days before adriamycin injection and daily thereafter for 72 hours resulted in a significant decrease in both plasma cholesterol and triglycerides compared to their respective adriamycin injected rats .

(B) Histological examination of heart sections under light microscope :

Examination of heart sections under light microscope after 72 hours of adriamycin injection revealed sporadic early necrotic fibers , highly eosinophilic cytoplasm , vascular congestion , interstitial oedema , mononuclear cellular infiltration and intravascular hemolysis . Pre treatment of adriamycin injected rats with silymarin 7 days before adriamycin injection and daily thereafter for 72 hours of adriamycin injection resulted in mild interstitial oedema , vascular congestion and little subendocardial cellular infiltration .

(C) Electron microscopic examination (ultra structural study) :

Examination of heart sections by electron microscope in adriamycin injected rats revealed degeneration and loss of myocardial fibers , numerous cytoplasmic vacuoles in-between the myofilaments , swollen enlarged mitochondria . Pre treatment of adriamycin injected rats with silymarin revealed that these changes are mild .

The results of the present work reported that silymarin may protect against adriamycin cardiac toxicity .