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Cardioprotective effect of thymoquinone, an active principle of *Nigella sativa*, on isoproterenol induced myocardial injury

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Myocardial injury constitutes a major cause of morbidity and mortality in humans. Medicinal plants have recently been acclaimed to be a rich source of therapeutic potential. *Nigella sativa* (*N. sativa*) seed and its active principles were shown to possess many biological effects, including antioxidant properties. In the present study, thymoquinone (TQ), an active principle of *N. sativa*, was investigated for its possible protective role in the isoproterenol induced myocardial injury, which is a classical example of the excess catecholamines related myocardial hypoxia, angina, acute coronary insufficiency as well as 'stress cardiomyopathy'. Male Wistar albino rats, weighing between 150 and 300 g were used for the study. TQ, dissolved in olive oil, was administered orally in doses of 12.5, 25 and 50mg/kg to three groups of rats (n=4 in each group), for 7 days and the two control groups (n=4) were given only plain olive oil. Thereafter, TQ receiving groups and one control group (Active controls) were injected, subcutaneously, with isoproterenol 125mg/kg for 2 days. Myocardial injury was assessed by biochemical markers (plasma LDH, TBARS, GR & SOD and myocardial GSH/GSSG ratio) as well as histopathology. Biochemical parameters were expressed as mean \pm SD and variability of different groups was estimated by one way ANOVA followed by Bonferroni test. In controls given olive oil only (Passive controls) plasma LDH, TBARS and GR activity was 689 ± 103 (U/L), 3.4 ± 0.57 (μ mole/L) and 20.11 ± 1.34 (nmole/min/ml), respectively; while these parameters increased to 3521 ± 43 , 5.95 ± 0.72 and 79.31 ± 28.7 , respectively, in controls receiving isoproterenol ($P < 0.001$, 0.003 and 0.007). There was a dose related decrease in these markers in TQ treated groups down to the levels of passive controls with TQ 50mg/ml (935 ± 123 , 3.7 ± 0.25 and 17.43 ± 3.35 ; $P < 0.001$, 0.01 , 0.005 as compared with active controls). Decrease in the plasma SOD (U/ml) and the myocardial GSH/GSSG ratio produced with isoproterenol (0.048 ± 0.002 and 9.88 ± 0.25 , respectively) was also reversed in a dose related manner in TQ treated rats close to the levels of passive controls (0.15 ± 0.02 and 33.56 ± 2.61 , respectively) with TQ 50mg/ml (0.16 ± 0.019 and 32.22 ± 2.84 ; $P < 0.001$ in both cases when compared with active controls). The histological changes caused by isoproterenol in active controls were also reversed in TQ treated groups. The results of our study revealed the cardioprotective effect of TQ, the most abundant active principle of *N. sativa*, in the isoproterenol-induced myocardial injury. The regular use of *N. sativa* seed is suggested for the prevention of ischemic heart disease.