Thymoquinone Dose-Dependently Attenuates Myocardial Injury Induced by Isoproterenol in Rats Via Integrated Modulations of Oxidative Stress, Inflammation, Apoptosis, Autophagy, And Fibrosis

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Abstract

As rats develop myocardial infarction (MI) like lesions when injected with large doses of isoproterenol (ISO), this investigation was designed to evaluate the dose-dependent effects of thymoquinone (TQ) on ISO-induced myocardial injury in rats.

Methods

Adult male rats were divided into negative control, TQ20 (20 mg/kg/day), TQ50 (50 mg/kg/day), ISO positive control, TQ20+ISO, and TQ50+ISO groups. In these rats, biochemical, immune biochemical, and histopathological studies were carried out to evaluate myocardial oxidative stress, inflammation, apoptosis, fibrosis, and autophagy, and the changes in serum cardiac biomarkers.

Results

The results showed that TQ pretreatment in ISO-administered rats produced a dose-dependent significant reduction of the myocardial infarct size, markedly reduced the ISO-induced elevation in serum cardiac markers and demonstrated several other important findings related to the cardioprotective efficacy of TQ. First, this study is the first reported research work showing that TQ treatment could increase the myocardial reduced glutathione baseline level, adding an indirect antioxidant effect to its known direct free radical scavenging effect.

Second, pretreatment with TQ significantly reduced the markers of myocardial oxidative stress, inflammation, fibrosis, and apoptosis. Third, TQ acted as an autophagy enhancer ameliorating myocardial cell damage and dysfunction. Thus, the morphological and biochemical changes associated with ISO-induced myocardial injury were ameliorated with TQ pretreatment. The extent of this improvement was significantly greater in the TQ50+ISO group than in the TQ20+ISO group. The present study, for the first time, demonstrates these dose-dependent effects of TQ in experimentally induced myocardial injury. These findings raise the possibility that TQ may serve as a promising prophylactic cardioprotective therapy for patients who are at risk of developing myocardial injury and against the progression of existent myocardial injury as in cases of MI.

***Keywords*:**

Myocardial infarction · Thymoquinone · Oxidative stress · Inflammation-fibrosis · Apoptosis · Autophagy.