

Protective Effect of *Cinnamomum zeylanicum* Bark Extract against Doxorubicin Induced Cardiotoxicity: A Preliminary Study

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Abstract : Introduction: Doxorubicin is widely used in the treatment of solid organ tumors and hematological malignancies, but the dose-dependent cardiotoxicity due to free radical formation compromises its clinical utility. Therapeutic strategies which enhance cellular endogenous defense systems have been identified as promising approaches to combat oxidative stress-associated conditions. *Cinnamomum zeylanicum* (Ceylon cinnamon) has a number antioxidant compounds, which can effectively scavenge reactive oxygen including superoxide anions, hydroxyl radicals and as well as other free radicals. Therefore, the objective of the study was to elucidate the most effective dose of *Cinnamomum* bark extract which ameliorates doxorubicin-induced cardiotoxicity. Materials and methods: Wistar rats were divided into seven groups of 10 animals in each. Group 1: normal control (distilled water, orally, for 14 days, 10 mL/kg saline, ip, after 16 hours fast on the 11th day); Group 2: doxorubicin control (distilled water, orally, for 14 days, 18 mg/kg doxorubicin, ip, after 16 hour fast on the 11th day); Groups 3-7: five doses of freeze dried aqueous bark extracts (0.125, 0.25, 0.5, 1.0, 2.0g/kg, orally, daily for 14 days, 18 mg/kg doxorubicin, ip, after 16 hours fast on the 11th day). Animals were sacrificed on the 15th day and blood was collected for the estimation of cardiac troponin I (cTnI), AST and LDH concentrations and myocardial tissues were collected for histopathological assessment of myocardial damage and irreversible changes were graded by developing a score. Results: cTnI concentration of groups 1-7 were 0, 161.9, 128.6, 95.9, 38, 19.41 & 12.36 pg/mL showing significant differences ($p<0.05$) between group 2 and groups 4-7. In groups 1-7, serum AST concentration were 26.82, 68.1, 37.18, 36.23, 26.8, 26.62 & 22.43U/L and LDH concentrations were 1166.13, 2428.84, 1658.35, 1474.34, 1277.58, 1110.21 & 974.40U/L and a significant difference ($p<0.05$) was observed between group 2 and groups 3-7. The maximum score for myocardial necrosis was observed in group 2. Parallel to the increase of the dosage of plant extract, a gradual reduction of the score for myocardial necrosis was observed in groups 3-7. Reversible histological changes such as vacuolation, congestion were observed in group 2 and all plant treated groups. Haemorrhages, inflammatory cell infiltrations, and interstitial oedema were observed in group 2, but absent in groups treated with higher doses of the plant extract. Discussion & Conclusion: According to the in vitro antioxidant assays performed, *Cinnamomum zeylanicum* (Ceylon cinnamon) bark possesses high amounts of polyphenolic substances and high antioxidant activity. The present study showed that *Cinnamomum zeylanicum* extract at 2.0 g/kg possesses the most significant cardioprotective effect against doxorubicin-induced cardiotoxicity. It can be postulated that pretreatment with *Cinnamomum* bark extract may replenish the cardiomyocytes with antioxidants that are needed for the defense against oxidative stress induced by doxorubicin.

Keywords : cardioprotection, *Cinnamomum zeylanicum*, doxorubicin, free radicals

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