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Aqueous bark extract of *Nauclea orientalis* (Bak mee) attenuates doxorubicin induced inflammation and apoptosis in Wistar rats

Sandamali JAN^{1*}, Hewawasam RP², Jayatilaka KAPW², Mudduwa LKB³

¹Department of Medical Laboratory Science, Faculty of Allied Health Sciences, University of Ruhuna, Sri Lanka, ²Department of Biochemistry, Faculty of Medicine, University of Ruhuna, Sri Lanka, ³Department of Pathology, Faculty of Medicine, University of Ruhuna, Sri Lanka.

Background: Doxorubicin is an effective chemotherapeutic agent against solid organ tumors and haematologic malignancies. But, clinical effectiveness is largely limited by dose dependent cardiotoxicity as it was reported that administration of doxorubicin induces oxidative-stress, inflammation and apoptosis prominently in heart tissues. Previously, it has been reported that therapeutic agents with antioxidant activities significantly reduce cardiac dysfunction caused by doxorubicin. *Nauclea orientalis* is a medicinal plant which has significant antioxidant activities.

Objective: To investigate effect of *Nauclea orientalis* aqueous bark extract against doxorubicin-induced inflammation and apoptosis in Wistar rats.

Method: Five groups of healthy male and female Wistar albino rats were randomly divided; Group 1: normal-control; group 2: plant control; group 3 received dH₂O 14 days, doxorubicin (18mg/kg) on 11th day; group 4 received lyophilized plant extract (2.0g/kg) 14 days, doxorubicin (18mg/kg) on 11th day; group 5: dH₂O 14 days, dexrazoxane (180mg/kg) 0.5h before doxorubicin (18mg/kg). Animals were sacrificed on day 15; blood was collected to estimate myeloperoxidase (MPO) activity; myocardial tissues were examined after H&E staining and immunohistochemical staining for TNF- α , caspase-3, Bcl2 and Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay.

Results: Doxorubicin-treated group showed increased level of MPO activity (285.3 \pm 1.6 AAU/mL) and histological evidence of early changes of necrosis in a large area of the myocardium whereas plant-treated group showed significant reduction (p<0.05) in MPO activity (210.5 \pm 4.6 AAU/mL) and early changes of necrosis only in a smaller area. Expression of TNF- α and caspase-3 were more pronounced but Bcl2 expression was weak in the doxorubicin control. Plant-treated group showed significant reduction (p<0.05) in TNF- α and caspase-3 expression and increased Bcl-2 expression. TUNEL positive nuclei were abundant in the doxorubicin control but they were significantly reduced (p<0.05) in plant treated group.

Conclusion: *Nauclea orientalis* bark extract has the potential to attenuate doxorubicin-induced inflammation and apoptosis in Wistar rats.

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