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Conference Paper · February 2022

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A novel polyherbal formulation for the management of oxidative stress and inflammation in doxorubicin-induced nephrotoxicity

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Background: Herbal formulations provide desirable therapeutic effects in the management of drug-induced nephrotoxicity, which often demands remedial approaches with multiple protective effects. In this context, polyherbal formulations offer an invaluable resource due to their potential bio-interactions within and between the constituents.

Objective/s: The present study aimed to evaluate the efficacy of a novel polyherbal formulation derived from the leaves of *Abelmoschus moschatus* Medik. (Kapukinissa), *Asparagus falcatus* (L.) (Hathawariya), and whole plant of *Barleria prionitis* (L.) (Katukaradu), in ameliorating doxorubicin-induced nephrotoxicity via selected biomarkers of oxidative stress and inflammation.

Methodology: There were six groups in the study; healthy control group, doxorubicin-induced nephrotoxic control group, three polyherbal formulation treated groups at three selected doses and a positive control group. The polyherbal formulation was made of the aqueous refluxed (4h) extract of equal quantities (1:1:1 by weight) of the three selected medicinal plants. The aqueous polyherbal formulation at the 200, 400 (therapeutic dose), and 600 mg/kg doses (treatment groups) and the standard drug; fosinopril at 0.09 mg/kg dose (positive control group) were administered orally to doxorubicin-induced (5 mg/kg) nephrotoxic male Wistar rats for 28 consecutive days. The kidney tissues were excised at the end, for the biochemical and immunohistochemical assessments. The results of treatment groups were compared with the doxorubicin-induced nephrotoxic control group (n=6/group).

Results: Treatment with 400 and 600 mg/kg doses of the polyherbal formulation mitigated doxorubicin-induced oxidative stress by restoring antioxidant potential, as demonstrated by significantly increased levels of total antioxidant status (15%, 21%), glutathione reductase (61%, 102%) and glutathione peroxidase (18%, 45%) activities and decreased malondialdehyde formation (25%, 26%) in kidney homogenates ($p<0.05$). A reduction in the concentrations of TNF-α (40%, 35%) ($p<0.05$), IL-1β (36%, 42%) ($p>0.05$) and the immunohistochemical expression of COX-2 were observed, signifying potential anti-inflammatory effects. Immunohistochemical expression of BCL-2 (anti-apoptotic protein) was increased while Bax (pro-apoptotic protein) was reduced in the treatment groups compared to the doxorubicin-induced nephrotoxic control.

Conclusions: The findings revealed that the polyherbal formulation at 400 and 600 mg/kg doses attenuate doxorubicin-induced nephrotoxicity via antioxidant, anti-inflammatory, and anti-apoptotic pathways.

Keywords: *Polyherbal Formulation, Doxorubicin-Induced Nephrotoxicity, Antioxidant Effects, Anti-Inflammatory Effects, Anti-Apoptotic Effects*