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Citrullus colocynthis leaves extract protects against oxidative stress and inflammation induced by doxorubicin toxicity in rats

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Normal native practices usually take herbs with orthodox drugs for treatment and management of cancer. This study investigated the effects of *Citrullus colocynthis* methanol leaf extract in combination with doxorubicin (DOX). 24 male Wistar rats weighing averagely 150-200 g were randomly selected into four groups- A-D: Group A (control), B (administered 100 mg/kg body weight of extract), C (administered 0.35 mg therapeutic dose of DOX once daily at three days interval), D (combination of therapeutic dose of DOX with 100 mg/kg of extract). Malondialdehyde (MDA), reduced glutathione (GSH) concentrations as well as superoxide dismutase (SOD) and catalase (CAT) activities were determined in the heart and liver homogenates of the rats. Serum total protein (TP), pack cell volume (PCV), white blood cell count (WBC), C-reactive protein (CRP) and tumor necrosis factor alpha (TNF-α) were evaluated using standardized methods after administration for 15 days. Results showed that heart and liver antioxidant indices (GSH levels ,CAT and SOD activities) were significantly ($p<0.05$) increased with corresponding decreases in MDA levels in group treated with extract only while this was reversed in the group treated with DOX only. However, extract elicit a protective effect against doxorubicin in group D (DOX and extract) as levels and activities of these markers were restored nearly to the controls. Also, doxorubicin significantly ($p<0.05$) increased the serum levels of WBC, CRP, TP, and TNF-α while it significantly decreased PCV levels. Treatment with extract in group D showed significant reversal of this trend. Results revealed DOX induction of hepatic and cardiac toxicity, suggestive of oxidative stress and inflammation and the protective potential of extract against these effects. Hence, use of the extracts as supplement for cancer therapy could be encouraged as possible modulatory agent.

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Apoptotic effects of holamine and funtumine on selected cancer cell lines and their underlying mechanism of action

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Holamine and funtumine cytotoxicity and cell cycle arrest had been previously reported. The present study evaluates the apoptotic effects, reactive oxygen species (ROS) induction, mitochondrial depolarization, caspase-3 induction, F-actin perturbation of the two steroidal alkaloids in cancer cell lines (HT-29, MCF-7 and HeLa) and inhibition of topoisomerase-1. Apoptotic effect was studied by flow cytometry using the APOPercentage™ dye, Annexin-V/PI stain and induction of caspase-3 using the Caspase-3/7 Glo assay kit. Furthermore, ROS generation, mitochondrial perturbation, F-actin and topoisomerase-1 relaxation assay were evaluated following standard procedure. The two steroidal alkaloids were found to be more cytotoxic to cancerous cell than non-cancerous fibroblast. The cytotoxicity of the two alkaloids was mediated through induction of apoptosis. The apoptotic activation was found to be triggered by the activation of caspase-3, induced ROS, mitochondrial toxicity, F-actin disorganization and topoisomerase-1 inhibition. The study relates the cytotoxicity activities of the two compounds for the stimulation of apoptosis pathway through induction of ROS, mitochondrial depolarization, F-actin disorganization and topoisomearase-1 inhibition.

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