

## EFFECTS OF *GLOBULARIA ALYPUM* EXTRACTS ON DOXORUBICIN-INDUCED OXIDATIVE STRESS IN RAT'S HEART AND THEIR INFLUENCE ON HepG2 CELL VIABILITY

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### ABSTRACT:

*Globularia alypum* L. (GA) a perennial shrub found throughout the mediterranean area. It is one of the most traditional plant remedies, its leaves are traditionally used as hypoglycaemic agent, laxative, cholagogue, stomachic, purgative and sudorific. It is also used in the treatment of cardiovascular and renal diseases. Recently, hydroalcoholic extracts of GA aerial parts were also shown a significant antioxidant effect. A significant antileukemic activity of an aqueous extract of GA (GAAE) was also reported. Doxorubicin (DOX) is an efficient chemotherapeutic agent used against several types of tumors; however, its use is limited due to severe cardiotoxicity. Since it is accepted that DOX induced myocardopathy is the consequence of oxidative stress through the mediation of free radicals, antioxidant agents have been used to attenuate its side effects. The aim of this study was to investigate the effect of the aerial parts butanolic extract of GA (GABE) on the acute cardiac toxicity induced by DOX in rats as well as the anti-proliferative activity of the aqueous extract on human hepatocarcinoma cell line (Hep G2). The analytical chemical study showed the phenolic nature of GABE. In Vitro the GABE exhibited a significant antioxidant activity, based on the scavenging activity of the stable free radical DPPH° where the IC<sub>50</sub> was 0.021 mg/ml. Oxidative stress in the heart tissue was estimated by measuring the glutathione (GSH) levels and malondialdehyde (MDA) in the homogenate. The pretreatment of rats with the GABE orally at a dose of 100mg/kg for a month resulted in a decrease in the cardiac cytosolic MDA and maintenance of cardiac cytosolic GSH level as compared to DOXO treated animals at a dose of 20 mg/kg intraperitoneally. Using MTT Cell Viability assay, the GAAE showed a cytotoxic effect against Hep G2 cells as indicated by its low IC<sub>50</sub> value 43.82 µg/ml. These results provide preliminary experimental evidence supporting the use of GA against hepatocellular carcinoma and open the possibility of considering this plant an adjunctive medicine for the treatment of this deadly disease. and may be a useful agent in the combination therapy with DOXO to limit free-radical-mediated cardiac injury.

**KEY WORDS:** *Globularia alypum*, Doxorubicin, oxidative stress, cardiotoxicity, antioxidant, HepG2, cytotoxicity.