**ABSTRACT**

Despite the recent development of target-specific innovative agents, cytotoxic agents still remain the milestone of anticancer therapy. Unfortunately, their toxicity and drug resistance are major clinical obstacles to the effective treatment of tumor acidicmicroenvironment in cancer development, progression, and metastasis. As a consequence, the need for compounds that specifically target the mechanism responsible for the low pH of tumors is increasing. Hence, we investigated whether anti-acid pantoprazole could inhibit the acidification of the tumor microenvironment and increase the sensitivity of cancer cells to cytotoxic Cytarabine. HL-60 cell line were treated with Pantoprazole (100,200,400μg/ml) alone and in combination with Cytarabine showed significant dose and time dependent decrease in percentage cell viability as compared to control in MTT, Trypan blue exclusion assay and clonogenic assay, DNA fragmentation in dose dependent manner. but the effect of their combination showed only DNA fragmentation and not the caspase-3 enzyme. The higher doses of their combination showed paradoxical effect in presence of caspase-3 enzyme. The study was also done on DLA induced mice were treated with pantoprazole (40 mg/kg, 80mg/kg) alone and in combination with Cytarabine(100mg/kg) for 8 and 16 days were we recorded that there was significant deacrease in reduced glutathione level and in nitric oxide, LDH level were increased, volume of peritoneal cell, packed cell volume were decreased significantly in dose and combination dependent manner in all treated groups compared to tumour induced control group. The combinations maintained the normal levels of leukocytes, platelet, and haemoglobin content. Thus Pantoprazole showed very significant anticancer effect in dose and time dependent manner and showed synergistic anticancer effect with Cytarabine and also reduced adverse effects of Cytarabine.

**Keywords:** Anticancer therapy, drug resistance, tumour acidic microenvironment, clonogenic assay, pantoprazole, , DNA fragmentation, caspase-3 enzyme, Cytarabine