

## **Bromelain enhances the anti-tumor effects of cisplatin on 4T1 breast tumor model in vivo**

### **ABSTRACT**

**Background:** This study aimed to evaluate the antitumor enhancing effect of bromelain consumption on 4T1-challenged mice treated with cisplatin. **Methods:** Mice challenged with 4T1 triple-negative breast cancer cells received water, bromelain, cisplatin, or bromelain + cisplatin treatment for 28 days. Tumor size was measured, and lung metastasis was evaluated by clonogenic assay. Expression of tumor inflammatory genes of the harvested tumor was quantified by polymerase chain reaction array and ELISA (enzyme-linked immunosorbent assay). **Results:** All treatments significantly reduced the size of tumor and lung metastasis, with combination treatment showing the best effect. Also, bromelain alone and combination treatment showed downregulation of the expression of tumor inflammatory genes (Gremlin [GREM1], interleukin 1 $\beta$  [IL-1 $\beta$ ], interleukin-4 [IL-4], nuclear factor  $\kappa$ B subunit 1 [NF $\kappa$ B1], and prostaglandin-endoperoxide synthase 2 [PTGS2]), tumor nitric oxide level, and serum IL-1 $\beta$ , and IL-4 levels. On the other hand, cisplatin treatment increased the expression of selected inflammatory markers. **Conclusion:** This study suggests that bromelain treatment could potentiate the antitumor effect of cisplatin on triple-negative breast cancer 4T1 cells through modulating the tumor environmental inflammation.

**Keyword:** Antitumor; Bromelain; Cisplatin; Inflammation; In vivo