

Apoptosis and metastasis inhibitory potential of pineapple vinegar against mouse mammary gland cells in vitro and in vivo

Abstract

Background: Plant-based food medicine and functional foods have been consumed extensively due to their bioactive substances and health-beneficial effects. Vinegar is one of them due to its bioactivities, which confers benefits on human body. Our previous study has produced pineapple vinegar that is rich in gallic acid and caffeic acid via 2 steps fermentation. There are many evidences that show the effectiveness of these resources in inhibiting the proliferation and metastasis of the cancer cells through several mechanisms. Methods: Freeze-dried pineapple vinegar was evaluated for its in vitro apoptosis and metastasis inhibitory potential using MTT, cell cycle, Annexin V and scratch assays. The in vivo test using BALB/c mice challenged with 4 T1 cells was further investigated by pre-treating the mice with 0.08 or 2 ml/kg body weight of freshly-prepared pineapple vinegar for 28 days. The tumor weight, apoptotic state of cells in tumor, metastasis and immune response of the untreated and pineapple vinegar treatment group were evaluated and compared. Results: From the in vitro study, an IC₅₀ value of 0.25 mg/mL after 48 h of treatment was established. Annexin V/PI and scratch closure assays showed that pineapple vinegar induced 70% of cell population to undergo apoptosis and inhibited 30% of wound closure of 4 T1 cells. High concentration of pineapple vinegar (2 ml/kg body weight) led to the reduction of tumor weight and volume by 45% as compared to the untreated 4 T1-challenged mice. This effect might have been contributed by the increase of T cell and NK cells population associated with the overexpression of IL-2 and IFN- γ cytokines and splenocyte cytotoxicity. Furthermore, fewer instances of metastasis events were recorded in the pineapple vinegar treatment group and this could be explained by the downregulation of inflammation related genes (iNOS, NF- κ B and COX2), metastasis related genes (iCAM, VEGF and MMP9) and angiogenesis related genes (CD26, TIMP1, HGF, MMP3, IGFBP-1 and IGFBP-2). Conclusion: The ability of pineapple vinegar to delay cancer progression portrayed its potential as chemopreventive dietary intervention for cancer therapy.