

The cytotoxic effect and glucose modulation of *Baekkea frutescens* on breast cancer cells

ABSTRACT

Background: *Baekkea frutescens* (*B. frutescens*) of the family Myrtaceae is a plant that has been used in traditional medicine. It is known to have antibacterial, antipyretic and cytoprotective properties. The objective of this study is to explore the mechanism of *B. frutescens* leaves extracts in eliminating breast cancer cells. Method: *B. frutescens* leaves extracts were prepared using Soxhlet apparatus with solvents of different polarity. The selective cytotoxicity of these extracts at various concentrations (20 to 160 $\mu\text{g/ml}$) were tested using cell viability assay after 24, 48 and 72 h of treatment. The IC_{50} value in human breast cancer (MCF-7 and MDA-MB-231) and mammary breast (MCF10A) cell lines were determined. Apoptotic study using AO/PI double staining was performed using fluorescent microscope. The glucose uptake was measured using 2-NBDG, a fluorescent glucose analogue. The phytochemical screening was performed for alkaloids, flavonoids, tannins, triterpenoids, and phenols. Results: *B. frutescens* leaves extracts showed IC_{50} value ranging from 10 -127 $\mu\text{g/ml}$ in MCF-7 cells after 72 h of treatment. Hexane extract had the lowest IC_{50} value (10 $\mu\text{g/ml}$), indicating its potent selective cytotoxic activity. Morphology of MCF-7 cells after treatment with *B. frutescens* extracts exhibited evidence of apoptosis that included membrane blebbing and chromatin condensation. In the glucose uptake assay, *B. frutescens* extracts suppressed glucose uptake in cancer cells as early as 24 h upon treatment. The inhibition was significantly lower compared to the positive control WZB117 at their respective IC_{50} value after 72 h incubation. It was also shown that the glucose inhibition is selective towards cancer cells compared to normal cells. The phytochemical analysis of the extract using hexane as the solvent in particular gave similar quantities of tannin, triterpenoids, flavonoid and phenols. Presumably, these metabolites have a synergistic effect in the in vitro testing, producing the potent IC_{50} value and subsequently cell death. Conclusion: This study reports the potent selective cytotoxic effect of *B. frutescens* leaves hexane extract against MCF-7 cancer cells. *B. frutescens* extracts selectively suppressed cancer cells glucose uptake and subsequently induced cancer cell death. These findings suggest a new role of *B. frutescens* in cancer cell metabolism.

Keyword: *Baekkea frutescens*; Glucose uptake; Apoptosis; Oxidative phosphorylation; Breast cancer