

The cytotoxic effect of *Baekkea frutescens* extracts in eliminating hypoxic breast cancer cells

ABSTRACT

Background: Adaptive metabolic response towards a low oxygen environment is essential to maintain rapid tumour proliferation and progression. The vascular network that surrounds the tumour develops an intermittent hypoxic condition and stimulates hypoxia-inducing factors. *Baekkea frutescens* is used in traditional medicine and known to possess antibacterial and cytoprotective properties. In this study, the cytotoxic effect of *B. frutescens* leaves and branches extracts against hypoxic human breast cancer (MCF-7) was investigated. **Method:** The extracts were prepared using Soxhlet apparatus for ethanol and hexane extracts while the water extracts were freeze-dried. In vitro cytotoxic activities of *B. frutescens* extracts of various concentrations (20 to 160 µg/mL) at 24, 48, and 72 hours time points were studied using MTT in chemically induced hypoxic condition and in 3-dimensional in vitro cell culture system. An initial characterisation of *B. frutescens* extracts was carried out using Fourier-transform Infrared- Attenuated Total Reflection (FTIR-ATR) to determine the presence of functional groups. **Results:** All leaf extracts except for water showed IC₅₀ values ranging from 23 -158 µg/mL. Hexane extract showed the lowest IC₅₀ value (23 µg/mL), indicating its potent cytotoxic activity. Among the branch extracts, only the 70% ethanolic extract (B70) showed an IC₅₀ value. The hexane leaf extract tested on 3- dimensional cultured cells showed an IC₅₀ value of 17.2 µg/mL. The FTIR-ATR spectroscopy analysis identified various characteristic peak values with different functional groups such as alcohol, alkenes, alkynes, carbonyl, aromatic rings, ethers, ester, and carboxylic acids. Interestingly, the FTIR-ATR spectra report a complex and unique profile of the hexane extract, which warrants further investigation. **Conclusion:** Adaptation of tumour cells to hypoxia significantly contributes to the aggressiveness and chemoresistance of different tumours. The identification of *B. frutescens* and its possible role in eliminating breast cancer cells in hypoxic conditions defines a new role of natural product that can be utilised as an effective agent that regulates metabolic reprogramming in breast cancer.

Keyword: *Baekkea frutescens*; Hypoxia; Breast cancer; Apoptosis; 3-Dimensional cell culture