Bioassay-Guided Fractionation of Carica Papaya Leaf Juice Showing Selective Anti-Proliferative Activity on Prostate Cancer Cell

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Purpose
Cytotoxic drugs are widely used to eradicate cancer cells from the body. However, their dose-associated side effects and toxicity to non-tumor tissues limit their use. Therefore, selective alternative therapies against cancer with minimal or no effect over healthy tissues are highly desirable. Carica papaya (Caricaceae) leaves have a long history of nutritional and medicinal uses. Recent studies indicated the selective growth inhibitory properties of papaya leaf juice extract(s) (Pandey et al, 2015; Nguyen et al, 2016). In the present study, medium-polarity solvent extracts of C. papaya leaf juice were investigated for their anti-proliferative activity on a prostate cancer cell line (PC-3) and a prostatic stromal myofibroblast cell line (WPMY-1).

Methods
Papaya leaf juice (LJP) was collected from medium-sized mature papaya leaves, and extracted sequentially using hexane and ethyl acetate. The ethyl acetate solvent extract was further fractionated using semi-preparative HPLC equipped with diode array detection. The growth inhibitory activities of these subsequently vacuum-dried sub-fractions were examined using the CyQUANT cell proliferation assay and the results were expressed as IC50 values.

Results
The medium polarity (ethyl acetate) fraction of LJP (MP-LJP) displayed significant growth inhibitory effect on PC-3 cells (IC50 = 20 μg/mL), and interestingly did not show significant effect over proliferation responses of WPMY-1 cells. Further, individual sub-fractions of MP-LJP also showed selective growth inhibitory activity on PC-3 cells when compared to WPMY-1 cells. These sub-fractions, when used in a number of combinations, yielded significant anti-proliferative activity over PC-3 cells (IC50 = 17 μg/mL), whilst minimal effect was observed on the proliferation of WPMY-1 cells.

Conclusion
Our study has isolated papaya leaf juice fraction(s) and showed selective anti-proliferative activity of these fractions (and their combinations) in prostate cancer cells. Future investigations are required to identify the compounds responsible for selective growth inhibitory activity.