



Annona muricata extracts abrogate docetaxel induced cytotoxicity in normal prostate cells

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BACKGROUND

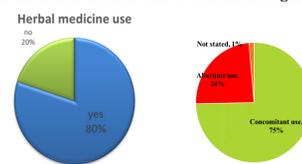
Prostate cancer has remained the leading cancer site in males in Jamaica for the past decade with the highest mortality and incidence rates. The high mortality rates among prostate cancer patients result from the prevalence of metastatic and aggressive castration resistant prostate cancer (CRPC) for which chemotherapy with docetaxel is the main treatment option. Docetaxel can cause significant adverse effects and even toxicity to normal cells, causing patients to seek natural products for an alternative therapeutic option. It is well known that cancer patients practice the use of medicinal plants therapeutically. A survey conducted among cancer patients at the University Hospital of the West Indies, revealed that *Annona muricata* was the most commonly used plant among cancer patients in Jamaica, with 59% of cancer patients reportedly using both the leaves and bark of the *A. muricata* plant prepared as either a decoction or an infusion to treat their cancer. It should also be noted that majority of the users were prostate cancer patients who used the plant concomitantly with chemotherapeutic drugs such as docetaxel. The impacts of such combinations are unknown and widely speculated to be negative. The cytotoxic impact *in vitro*, on prostate cancer and normal prostate cells treated with docetaxel alone and in combination with the extract, was investigated.

OBJECTIVES

In chemotherapy drugs are often combined to enhance anticancer efficacy. This therapeutic approach broadens therapeutic targets and result in a synergistic or additive anticancer effect; while contributing to overcoming drug resistance reducing toxicity. Our main objectives were to:

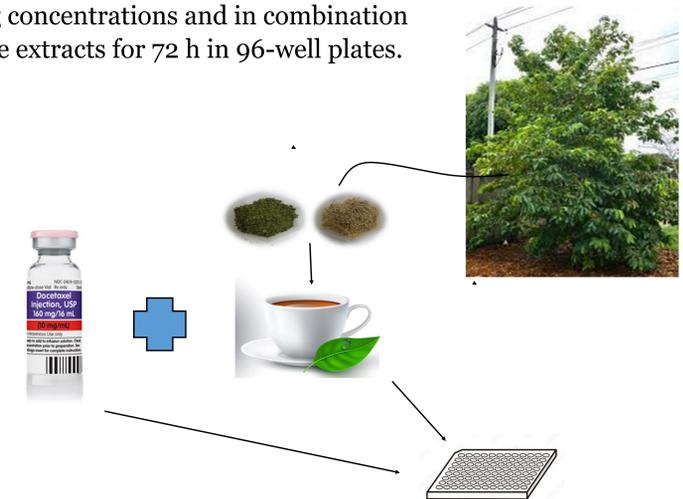
- ◆ Determine the cytotoxic impact of docetaxel on normal prostate cells.
- ◆ Investigate the impact of docetaxel applied in combination with *A. muricata* extracts on both prostate cancer and normal prostate cells.

Prevalence and practices of cancer patients who use herbal medicines in their cancer treatment regime



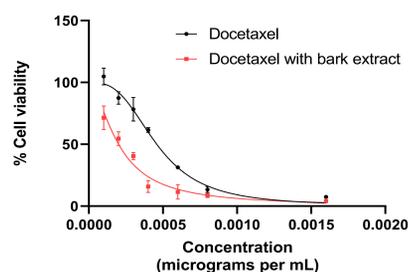
METHODS

The cytotoxic impact of docetaxel was evaluated in combination with *A. muricata* extracts using the MTS assay on cultured prostate cancer cell line (DU-145) and compared with its effect on a normal prostate cell line (RWPE-1). Cells were cultured until 95% confluence and subsequently treated with docetaxel at varying concentrations and in combination with the extracts for 72 h in 96-well plates.



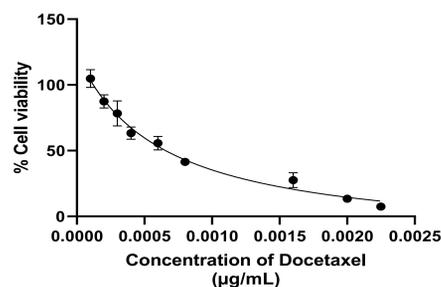
RESULTS

Docetaxel in combination with 100 µg/mL EAB extract against DU-145 prostate cancer



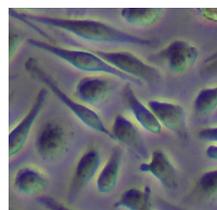
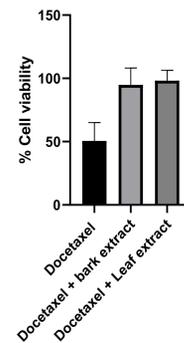
A greater impact on cell viability was obtained by combining docetaxel with bark extract. This resulted in a decrease of the IC₅₀ of docetaxel from 0.0004 to 0.0002 µg/mL within a 95% confidence interval. Combining docetaxel with the extract reduced the observed IC₅₀ by 50% rendering docetaxel twice as potent as when used alone.

RWPE-1

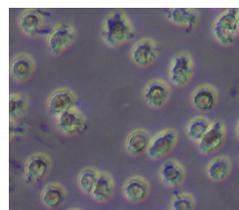


- Docetaxel displayed cytotoxicity against the normal prostate cell RWPE-1 with an IC₅₀ of 0.0006 µg/mL within a 95% confidence interval.
- Combining docetaxel with the *A. muricata* extracts reduced the cytotoxic impact and caused a significant increase in the cell viability.

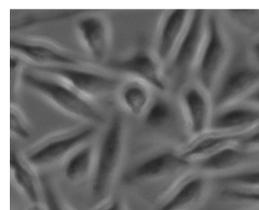
RWPE-1



RWPE-1 Cell Control



RWPE-1 treated with Docetaxel



RWPE-1 treated with Docetaxel and extract

CONCLUSIONS

A. muricata is commonly used concomitantly among Jamaican prostate cancer patients using medicinal plants. The scientific evidence suggests that it may hold promise as a viable adjuvant therapy for prostate cancer patients undergoing treatment with docetaxel. Therefore, our results support further evaluations for full characterization of this ethnomedical therapy to determine mechanisms of action and physiological relevance

REFERENCES

- Foster, K., Younger, N., Aiken, W., Brady-West, D., & Delgoda, R. (2017). Reliance on medicinal plant therapy among cancer patients in Jamaica. *Cancer Causes & Control*, 28(11), 1349-1356.
- Foster, Kimberley, et al. "Selective cytotoxic and anti-metastatic activity in DU-145 prostate cancer cells induced by *Annona muricata* L. bark extract and phytochemical, annonacin." *BMC Complementary Medicine and Therapies* 20.1 (2020): 1-15.

ACKNOWLEDGEMENTS

- Mr. Patrick Lewis at the UWI Mona herbarium for plant identification and collection.
- The Office of Graduate Studies & Research at the UWI Mona for funding to conduct research.