IN VITRO ANTI-PROLIFERATIVE EFFECTS OF THE *Nauclea orientalis* FRUIT ON ENDOMETRIAL CARCINOMA (AN3CA) CELLS

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1. Introduction

Cancer is a collection of heterogeneous genetic diseases characterized by alterations in multiple cellular signaling pathways that regulate cellular differentiation, survival, proliferation and death. There is an annual cost of $157 billion worldwide, for cancer care. Endometrial carcinoma is a common gynecological malignancy and a leading cause of cancer death in the world. The selected cell line for the present study (AN3CA) endometrial carcinoma has been identified as a type that is resistant to chemotherapy. In recent years herbal therapies are becoming preferred and a popular alternative in curing cancer including endometrial carcinoma as current therapeutic methods are implicated with many limitations and drawbacks. *Nauclea orientalis* is, a plant belonging to family Rubiaceae which is native to Australia, New Guinea and South East Asia reported to have a very high medicinal value. The trees bear bitter tasting, edible fruits eaten by Indigenous people of Australia (Aboriginal people). Studies carried out with the indole alkaloids from the ammoniacal extract of *N.orientalis* have reported to have *in vitro* anti-proliferative effect on human bladder carcinoma. However the anti-proliferative effect of *N.orientalis* fruit on endometrial carcinoma cells or any other cancer cells have not yet been evaluated. Therefore the present study designed to test the *in vitro* anti-cancer effects in the fruit of *N.orientalis* on endometrial carcinoma cells (AN3CA).

2. Research Methods

The flesh and peel of *N.orientalis* were freeze dried and sequentially extracted separately into four different solvents (hexane, dichloromethane, ethyl acetate and methanol). All eight extracts were dried under reduced pressure and different concentrations (0 – 200 µg/mL) of these extracts were exposed to endometrial carcinoma (AN3CA) cells. Anti-proliferative effects and induced apoptotic effects of all extracts were determined by Sulforhodamine B assay, light microscopic and florescence microscopic analysis of morphological changes respectively.

Image 1 – *Surface and cross-section of the fruit of N. orientalis*

3. Results

According to the obtained IC_{50} values of all eight extracts, flesh - dichloromethane (IC_{50}= 60.71 µg/mL) and flesh-ethyl acetate (IC_{50}= 89.56 µg/mL) extracts have exerted a potent anti-proliferative effect at 48 h post-incubation. Morphological changes exerted apoptotic changes in flesh - dichloromethane and flesh-ethyl acetate treated cells.

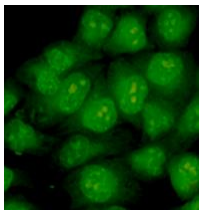

Image 2 – *Untreated control*

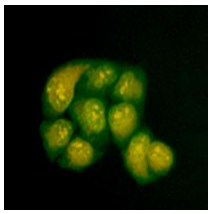

Image 3 – *Flesh-Dichloromethane (DCM-60 ppm)*

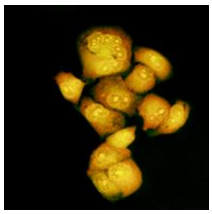

Image 4 – *Flesh-Dichloromethane (DCM-120 ppm)*

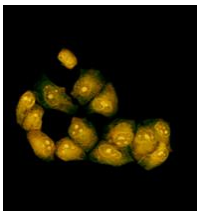

Image 5 – *Flesh-Ethyl acetate (EA-80 ppm)*

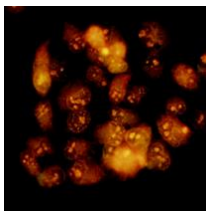

Image 6 – *Flesh-Ethyl acetate (EA-160 ppm)*

4. Conclusion

Collectively, both flesh - dichloromethane and flesh-ethyl acetate extracts of *N. orientalis* fruit, have significant anti-proliferative and apoptotic effect on chemo resistant endometrial carcinoma cells.

5. References

1. C.A.J. Erdelmeier, U. Regenass, T. Rali, O. Sticher Indole alkaloids with *in vitro* antiproliferative activity from the ammonical extract of *Nauclea orientalis*. 1992, *Planta Med*. 58(1), 43-8.
2. W.H. Talib Anticancer and Antimicrobial Potential of Plant-Derived Natural Products, *Phytochemicals – Bioactivities and Impact on Health*, 2011, *Intech Publication.*