

ABSTRACT

Biochemical Comparison of White Yam Biomaterials and Novel Synthesized Anticancer Compounds

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The development and identification of novel anticancer compounds may be achieved through two major routes, naturally or synthetically. The objective of this study was to identify new anticancer compound from *Dioscorea alata* cv White Yam tuber; chemically synthesizes novel anticancer compound using the thiosemicarbazone ligand and characterized the anticancer properties of these new compounds using a prostate cancer model. Chemoinformatic profiling of the Jamaican *D. alata* tuber identified anticancer activity within the acetone extract (DaJa-3). An enriched formulation of DaJa-3 was generated by a combination of SPE and HPLC fractionation (DaJa-3E3) and characterized by *in vitro* bioassay and GC-MS analysis. DaJa-3E3 possessed numerous saturated fatty acids, which inhibited the growth of DU-145 and A549 with an IC₅₀ of 31.45 µg/mL and 22.28 µg/mL. The inhibitory activity of DaJa-3E3 was mediated through apoptotic induction and cell cycle arrest. DaJa-3E3 induced growth arrest through G₁ blockage in DU-145 cells and by G₂ blockage in A549 cells. To increase the arsenal of anticancer compounds, novel di-2-thienyl ketone thiosemicarbazone (dtktsc) ligand was synthesized and complexed with zinc, copper, or palladium. The dtktsc and its metal complexes Zn(dtktsc)₂, Cu(dtktsc)₂ and Pd(dtktsc)Cl were structurally and biochemically characterized. Spectroscopic and elemental analysis provided evidence indicative of the proposed structures. Zn(dtktsc)₂ showed specificity towards LNCaP cells producing an IC₅₀ of 0.414µM after 24 hours exposure. The Cu(dtktsc)₂ had an effect on all cancer cell lines examined. However, it was most effective against LNCaP with an IC₅₀ of 1.583µM. The mechanism action of action of ligand metal complexes was assessed using flow cytometry, immunoblotting, and microscopic assessment. Using DU-145 cancer cells as a model, apoptosis induction by dtktsc, Zn(dtktsc)₂ and Cu(dtktsc)₂ was observed. There was a significant concentration and time dependent increase in apoptotic cells in DU-145 cells, accompanied by G₂/M cells arrest. Alltogether this study has identified two new important sources of anticancer compounds which are effective against prostate cancer cells.

Keywords: *Dioscorea alata*; Anticancer; Thiosemicarbazone; Acetone extract; Prostate cancer.