TOXICITY LEVEL ASSESSMENT OF VERNONIA AMYGDALINA EXTRACT AS COMPARED TO TRADITIONAL ANTI-CANCER DRUGS IN MCF-7 CELLS

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Abstract: The most useful chemotherapeutic agents act as monofunctional inducers. Such inducers modulate the expression of Phase 2 enzymes (protection and clearance) without affecting Phase 1 enzymes, which are involved in biotransformation. Prior studies have revealed that water-soluble Vernonia amygalina (VA) extracts treatment 1) inhibits growth of various cancer cell types without harmful side effects, 2) reverses ethonal-induced stimulatory responses in paclitaxel-sensitive human cancer cell growth, and 3) leads to increased microsomal epoxide hydrolase (Phase 2) gene product expression levels without affecting cytochrome P450 1A1/1A2 (phase 1) expression, thus supporting the chemotherapeutic potential of VA. Therefore, one objective of this study was to assess the growth-inhibitory activity of VA compared to three commonly used anti-cancer drugs: Paclitaxel (Taxol), Doxorubicin (Dox) and Vincristine (Vin) in the estrogen receptor positive breast cancer cell line MCF-7. Mitosis was determined by DNA synthesis assays and confirmed by cell counts using a hemacytometer. Exposure of MCF-7 cells to increasing concentrations of aqueous VA abrogated cell growth in a concentration-dependent fashion: VA at concentrations of 10 and 100 µg/ml inhibited MCF-7 cell viability (growth) by 25% (p<0.05) and 50% (p<0.05) respectively compared to the controls. Most notably, increasing concentrations of Taxol (10 & 100 nM), Vin (10 & 100 nM) and Dox (10 nM only), both alone and in combination with VA did not have any significant effect on DNA synthesis. However, Dox at 100 nM inhibited cell growth by 85%. These data suggest that MCF-7 cells are extremely sensitive to VA compared to either of the other drugs. Another objective of this study was to assay Phase 1 enzyme content by Western blotting and Phase 2 enzyme (Glutathione S-transferase) activity following the same drug treatment regimen. Western blotting showed immunoreactive bands on filters probed with CYP 2E1 after VA and Taxol treatments only, indicating that these drugs specifically induce this P450 isoform. CYP 1A1 was not induced by either drug regimen. Phase 2 Glutathione S-transferase (GST) assays revealed 1) the highest activity from 100 nM Taxol, 2) higher activity following VA 100 µg/ml treatment than 10 nM Taxol or VA 10 µg/mL and 3) no activity above background for either Vin 10 nM, Vin 100 nM, Dox 10 nM, or Dox 100 nM. Our studies suggest that VA may be a comparable, if not better alternative for patients than traditional drugs.

Keywords: Vernonia amygalina extracts, Cytochrome P450 enzyme, Vinca and taxane drugs, mitosis.

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