COMPARISON OF TOXICITY OF VERNONIA AMYGDALINA EXTRACT TO THAT OF OTHER ANTI-CANCER DRUGS IN MCF-7 CELLS

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Abstract: One hallmark of the most useful chemotherapeutic agents is that they function as monofunctional inducers. Such inducers lead to modulation in expression of Phase 2 enzymes without affecting Phase 1 enzymes. Phase 1 enzymes are relevant in cancer studies in that they are involved in biotransformation, while Phase 2 enzymes are involved in protection and clearance. Prior studies have revealed that water-soluble Vernonia amygdalina (V.A.) extract treatment 1) inhibits growth of various cancer cell types without harmful side effects, 2) reverses ethanol-induced stimulatory responses in Paclitaxel-sensitive human cancer cell growth, and leads to increased microsomal epoxide hydrolase (Phase 2) gene product expression levels (MCF-7 cell treatment with 10ug/ml of V.A. extract for 4 hrs), without affecting cytochrome P450 1A1/1A2 (Phase 1) expression, thus supporting the chemotherapeutic potential of V.A. In this study, V.A. was compared to three other anticancer drugs, Paclitaxel (Taxel), Doxorubicin, and Vincristine, as related to their effect on expression of the Phase 2 enzyme, Glutathione S-Transferase (GST). GSTs are ubiquitous multifunctional enzymes which play a role in cellular detoxification. They conjugate toxicants to glutathione and render them more water soluble. The two classes of GSTs are comprised of both cytosolic and microsomal enzymes. MCF-7 cells were cultured using either 10 or 100ug/ml of V.A., or 10 or 100 nM of either Taxel, Doxorubicin or Vincristine; and we assayed for levels of total GST activity (cytosolic or microsomal) by measuring the conjugation of 1-chloro-2,4-dinitrobenzene with reduced glutathione. The conjugation is accompanied by an increase in absorbance, which we measured at 380 nm at the 5, 10, 15 and 20 minute time points. The rate of increase is directly proportional to the GST activity in the sample, and is an indicator of the toxicity of the drug. Results indicate that cytosolic GST was expressed over background absorbance levels after 10 min, and was detected in only the samples treated with Taxel (100 ug/ml) and Doxorubicin (100 nM). By 15 min, cytosolic GST increased in the Doxorubicin (100 nM) sample and was first detected in the Vincristine (10 nM) sample. Mitochondrial GST was first detected at the 15 min time-point, and was seen only in the Vincristine (100 nM) sample. At the 20 min time-point, cytosolic GST continued to increase in the Taxel (100 ug/ml), the Doxorubicin (100 nM) and the Vincristine (10 nM) samples. Cytosolic GST was first detected in the Doxorubicin (10 nM) and the Vincristine (100 nM) samples at the 20 min time-point. Mitochondrial GST continued to increase in the Vincristine (100 nM) sample, and was first seen in the Vincristine (10 nM) sample after 20 min. Neither cytosolic nor mitochondrial GST activity was detected in either the Taxel (10 ug/ml) or either the samples treated with 10 or 100ug/ml of V.A., and indicator that low and Taxel and V.A. extract are not as toxic as the other drugs. Perhaps V.A. may be a useful agent against breast tumor cells which survive chemotherapy with Taxel.

Keywords: Ethanol, V. amygdalina extract, Vincristine, Doxorubicin, and Paclitaxel.

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