SENSITIVITY OF TAXOL-RESISTANT PROSTATE CANCEROUS CELLS TO AQUEOUS *Vernonia amygdalina* EXTRACTS

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Abstract: Cancer of the prostate (PC) is the second leading cause of cancer-related deaths in American men. According to the American Cancer Society (ACS), about 186,320 new cases of PC were diagnosed in 2009. Of these new cases, an estimated 30,870 cases were expected to occur in African American men. An estimated 28,660 men died in 2009 as a result of PC. Paclitaxel or Taxol (TAX) is one of the most common drugs used to treat CP. The side effects of TAX include, but not limited to, lowered resistance of infection, anemia, bruising or bleeding, tiredness and feeling weak, and diarrhea. The latter statement underscores the urgent needs for the discovery and development of novel anti-cancer and/or adjuvant agents to ameliorate the unwanted side effects of these chemotherapies. Plant-derived agents represent excellent sources for such novel and patient-friendlier anti-cancer and/or adjuvant agents. There is increasing evidence to show that *Vernonia amygdalina* (VA) may be one candidate for such agents. In vitro studies were conducted to evaluate the inhibition of cell growth using different concentrations of VA (0.01, 0.1, and 1mg/ml) and TAX (0.01, 0.1, and 1 µM) by altering the expression of pro-cancer and/or oncogenes molecules p53, AKT, MAPK, NF-κB, c-myc, and p-glycoprotein. Cell growth was determined by ³H-thymidine incorporation assays and confirmed by cell counts using a hemacytometer. Treatment of cells with increasing concentrations of VA (0.01, 0.1, and 1mg/ml) extracts inhibited DNA Synthesis by 12%, 45% (p<0.05), and 73% (p<0.01) respectively. Neither (0.01, 0.1, and 1 µM) Taxol had any significant effects on cell growth suggesting that PC-3 cells were sensitive to VA and resistant to TAX. Molecular studies were performed to uncover mechanisms mediated by VA and Taxol in PC-3 cells. Neither VA nor Taxol caused phosphorylation of p53, a tumor suppressor gene. AKT, MAPK, NF-κB, and cMyc are involved in tumor cell proliferation, survival, and metastasis. VA and Taxol increased/decreased AKT expression and MAPK expressions. 1mg/ml VA suppressed NFkB activation at different times (5, 15, 30, 45, 60 minutes) by 57, 48, 51, 53 and 60 % respectively. On the other hand, 1 µM Taxol suppressed NFkB activation at different times (5, 15, 30, 45, 60 minutes) by 56, 48, 50, 57, and 50 % respectively. 1 mg/ml VA increased/decrease c-Myc activity while 1µM Taxol upregulated cMyc activities in prostate carcinoma cells at different time intervals. P-glycoprotein, an ATP dependent membrane transporter protein, is stimulated in multidrug resistance. VA inhibited p-glycoprotein while Taxol stimulated basal ATPase providing evidence of VA sensitivity and Taxol resistance in PC-3 cells.