EFFECTS OF ATRAZINE, ARSENIC, CADMIUM AND NITRATE MIXTURE ON CELL CYCLE OF BREAST CELL LINES

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Abstract: Over the last two decades, a compelling body of evidence has identified the disruption of cell cycle control mechanisms as a common pathway in human cancer. The G1, S, G2, and M phases are sequentially transitioned in response to growth factor or oncogenic stimulation. Generally, elevated incidences of certain cancers in many industrialized countries have been cited as evidence of widespread exposure to chemical pollutants. Possible relationships may exist between xenoestrogens and the observed increase in hormone responsive cancers such as breast, prostate and testicular cancers. Studies have shown that Atrazine (ATZ) can induce aromatase activity in certain human cell systems in vitro and a recent study found that atrazine caused cell accumulation in the G2 phase of lymphocytes. Cadmium (Cd) has been classified as a human carcinogen by the International Agency for Research on Cancer. It has been considered as one of the causative agents for pulmonary, prostate and testicular cancers from several animal and epidemiological studies. Arsenic is a known human carcinogen and causes tumors of the skin, lung, liver, urinary bladder, prostate, and possibly other sites. Nitrate in manure and fertilizer runoff is under suspicion as an endocrine disruptor. Normal breast cells (MCF-10A) and breast cancer cells (MCF-7) were exposed to mixture of ATZ, Cd, As and NO3. The mixture of the chemicals was prepared using their maximum contaminant level (MCL) as a unit for concentration. After the exposure periods, nuclei were isolated by propidium iodide (PI) hypotonic lysis method. Approximately 20000 nuclei per sample were analyzed for each exposed concentration with BD FACSCalibur, equipped with 4-Color, USA. The percentage of nuclei of the cell cycle was calculated using Modfit LT 3.0 (Verity Software House Inc., Topsham, ME, USA). ANOVA followed by mean separation using LSD at $\alpha = 0.05$ was performed on the percentage of nuclei in the different phases of the cell cycle. Arsenic and cadmium showed similar impact on G0/G1 phases in both cell lines. Ten thousand ppb nitrate did significantly decrease the number of nuclei in the G0/G1 phase of MCF-7 cells, but showed a significant increase in MCF-10-A nuclei. Ten percent mixture has no effect on the G0/G1 and S phases while 100% and 1000% mixtures significantly increased the percentage of the nuclei in the G0/G1 phase in both cell lines. Atrazine showed a significant decrease in the nuclei in the S-phase. Ten ppb arsenic and 5 ppb cadmium showed the same effect on nuclei in the S-phase. Nitrate at MCL significantly increased the nuclei in the S-phase of MCF-7 by 50 % and a significant decrease was noticed in MCF-10A cells. Nuclei treated with 100%mixture and 1000% mixture showed significant decrease in the S-phase in both cell lines.

Keywords: Atrazine, Arsenic, Cadmium, Nitrate, Mixture, Cell Cycle Breast cell line