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Atrazine induced toxicity in lab animals

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ABSTRACT *Indiscriminate use of herbicides has negative impact on the quality of environment and ultimately on the animal and human population. Atrazine belongs to the group of chloro-s-triazine herbicides that are used for control of weeds in crops such as corn, soybeans and sugarcane (EPA, 2001). Owing to its ability to control broadleaf weeds, atrazine is the most widely used herbicide in India (Subramaniyan et al., 1991) The residues of atrazine are found in some crops like oat and maize (Norris and Fong, 1983), in soil (Goh et al., 1993), environmental water (Vidacek et al., 1994) and in drinking water (Ghosh and Philip, 2006). Atrazine is most frequently detected in ground and surface water (Koskinen and Clay, 1997). Experimental administration of Atrazine through various routes in lab animals produces multiple organ toxicity.*

INTRODUCTION

Atrazine is the most commonly used herbicide in the world (Hayes et al., 2002). Atrazine does not degrade significantly in ground water and in surface water. It has a half life of more than 200 days to 2 years (ATSDR 2003). Atrazine and their metabolites are relatively persistent in soil for several months.

The translocation of atrazine from soil and water to plants and aquatic animals, results in its entry into food chain and bioaccumulation. Chronic exposure of this herbicide leads to non-Hodgkin type lymphoma, multiple myeloma, and sarcoma in agricultural workers (Chiu et al., 2004). Since atrazine is now most commonly used in the world to control weeds therefore the relative risk and benefits of this herbicide must be compared to the existing herbicides. In this article we had tried to review few important toxic effects caused by atrazine.

Atrazine induced immuno toxicity

Cantemir et al., (1997) reported significantly increased percentage of lymphocytes expressing p53 protein in atrazine treated rats depending on dose and time of administration, when atrazine was administrated in different doses (2.7 and 5.4 mg/kg bwt), each dose once a day, 5 days per week, for 6 and 12 months. It was suggested that atrazine modifies the p53 expression, which could confirm the clastogenicity of atrazine.

Liskova et al., (2000) studied the immunotoxicity of atrazine in mice at dose rate of 100mg/ kg bwt orally for 10 days and they observed 16% and 25% decrease in the number of IgM plaque forming cells per million splenic cells and decrease in the splenic cellularity and thymus weight.

Karrow et al., (2007) administered atrazine orally (0, 24, 250 and 500 mg/kg bw) daily for 14 days in female mice and observed significantly increased number of splenic CD8+ T cells, cytotoxic T cells and mixed leukocyte responses and dose dependently reduced host resistance to B16F10 melanoma as well as decreased thymus and spleen weight, total spleen numbers and fixed macrophages.

Atrazine induced female reproductive toxicity

Wetzel et al., (1994) studied that lengthening of the estrous cycle, increased number of days in estrus or under the influence of exposure to estrogen, early onset of galactocele formation, early onset of mammary and pituitary tumor formation, and an increased incidence of mammary and pituitary tumors when dietary administration of atrazine was made to Fischer 344 and Sprague-Dawley female rats at 400 ppm throughout lifetime.

Peruzovic et al., (1995) studied the subtle neurobehavioral effects (increased spontaneous activity in females and increased performance in avoidance conditioning trials in males) in offspring of rat dams exposed to 120 mg/kg atrazine 6 times during a 12-day period that ended 4 weeks before the rats were bred. They reported that mechanism for this effect is unknown, but since atrazine is not thought to persist in tissues, it may be mediated through changes in the dam that later affect the offspring.

Cummings et al., (2000) noticed a significant decrease in body weight and increase in pre implantation losses in four strains of rat, when atrazine was administered at dose rate of 100-200mg/kg bwt orally during first 3 days of pregnancy.

Narotsky et al., (2001) administered the atrazine by gavage to Sprague-Dawley (SD), and Long Evans (LE) rats @ 0, 25, 50, 100, or 200 mg/kg/day on gestation days 6 to 10 and the dams were allowed to deliver and litters were examined postnatally. Full litter resorption (FLR) occurred only at 200 mg/kg and delayed parturition was seen at 100 mg/kg. Regarding maternal toxicity, weight loss observed at 25 mg/kg in dams. When atrazine was administered @ 200 mg/kg to F344 rats on days 11 through 15 (after the LH-dependent period of pregnancy), no FLR was seen. They further suggested that atrazine-induced FLR is maternally mediated, and consistent with loss of LH support of the corpora lutea.

Atrazine induced male reproductive toxicity

Kniewald et al., (2000) reported significantly decreased body weight and relative weight of ventral prostrate, testis, sperm motility, sperm number in epididymis. The histopathology of testis revealed cell disorganization, cell cluster together with spermatocytes and various degenerative changes. Electron microscopy evaluation of testis revealed vacuolated cytoplasm, reduced collagen fibers, irregular shaped leydig cell degenerative changes in sertoli cells when atrazine was administered intra peritoneally at the dose rate of 60 and 120 mg/kg bwt twice a week over 60 days in rat.

Simic et al., (2001) observed a significant decrease in epididymal sperm number and sperm mobility when atrazine was administered orally at dose rate of 3, 15 mg/kg bwt daily for 30 days in male rats.

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Sunny et al., (2008) observed a significant decrease in epididymal sperm count, spermatozoa viability, sperm motility and daily spermatozoa production along with increased induction of abnormal spermatozoa in dose dependant manner when atrazine was administered orally at the dose rate of 120 and 200 mg/kg bwt for seven days to male Wistar rats.

Atrazine induced genotoxicity

Thomas et al., (1997) reported significant increase in the number of micronuclei in polychromatic erythrocytes and decreasing PCE/NCE ratio when female mice were administered with single highest tolerated dose of atrazine @ 1400 mg/kg bwt.

Tennant et al., (2001) studied the dose related increase in DNA damage in leukocyte when atrazine was administered at the dose rate of 125, 250, 500 mg/kg bwt in mouse. The genotoxicity was assessed by using the alkaline single cell gel (SCG) assay.

Zeljezic and Garaj-Vrhovac (2004) conducted comet assay on blood and mouse organs (kidney, liver, bone marrow, and spleen) to evaluate possible genome damage caused by atrazine. Gesaprim was injected intraperitoneally once at two different doses viz., 1.08 ml/kg and 0.07 microl/kg containing atrazine @ 540 mg/kg and 3.5 x 10(-2) mg/kg bw. Mice were sacrificed 24 hours after treatment. Alkaline comet assay on the blood samples, kidney, liver, bone marrow and spleen tissues were performed. Significant increase in tail length of comet assay for all 5 tissues were observed in mice treated with Gesaprim compared to the control. DNA of kidney and liver showed largest increase in migration over electrophoresis.

Freeman and Rayburn (2006) reported significantly increasing cytotoxicity in Chinese hamster ovary cell line (CHO) when atrazine was inoculated at the dose rate of 0.001–1.1 mM. They also noticed significant increase in the percentage of nuclei in the S phase and decrease in the percentage of nuclei in the G2 phase in flow cytometry.

CONCLUSION

Atrazine exposure leads to immuno, reproductive and geno toxicity. To prevent adverse effects of atrazine, it should be used in limited dose for crop protection.

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