



Biochemical Effects of Treatments with Herbicide Atrazine in Male Albino Rats

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ABSTRACT: Environmental persistence and bioaccumulation of atrazine which belong to the Chloro -S-triazines may constitute a substantial concern in terms of health of humans. This research looked at, male albino rats with 195±5 g weights, were orally given doses of 0, 60, 150, and 300 mg a.i./kg b.w. atrazine, respectively, daily for 30 days. Analysis of liver, kidney functions, endocrine disorders, sperm account, sperm motility and body organs weights (absolute & relative) were evaluated. Through the study duration, rats were observed for general behavior, symptoms of toxicity and mortality. At the end of the study, rats were sacrificed by decapitation after 24 hr., from last treatment. Organs of tested male rats were rapidly doffed washed and weighted individually. Then, the organ / body weight ratios were calculated, and blood was collected from rats 24 hr., after the end of 30 days and subjected for the biochemical parameters. Atrazine with the tested doses served no apparent signs of toxicity or mortality of treated rats throughout the period of investigation (30 days). The findings revealed that oral administration of male albino rats with the tested doses of atrazine lowered body weight gains and sperm dynamics, while raised organs weights (except testes weight which was lowered, and did not affect absolute kidney weight), the levels of selected liver (except total protein and glucose contents which were decreased) and kidney biomarkers in treated rats compared to control animals. Concentrations of T₃ were increased significantly in a dose-dependent manner; concentrations of T₄ hormone were increased only with the highest tested dose in treated rats compared to control animals. In other terms, atrazine is toxic to the body, blood, liver and kidney functions of exposed rats, also as an endocrine disruptor chemical that longtime exposure of atrazine has been shown to have negative consequences on health of humans and the environment.

Keywords: Atrazine, sub-acute toxicity, physiological, haematological, biochemical, reproductive biomarkers.

INTRODUCTION

Undoubtedly, the use of pesticides can help protect crops and reduce yield losses; however, with the constant development of agricultural chemistry, these pesticide residues bring some potential hazards to the environment and human body. Egypt is one of the intensive pesticide use country in Africa. Quantities of pesticides used in Egypt are about 600 ton/annually (Environ. Affairs agency, Egypt; 2009), and the total imported agricultural pesticides in Egypt was 10241.66 ton in 2016 (ElSafoury, 2020). Atrazine (ATRZ) (: 6-chloro-4-N-ethyl-2-N-propan-2-yl-1,3,5-triazine-2,4-diamine) is a member of Chloro -S-triazine family herbicide that has been one of the most widely used herbicides to control broad leaved weeds and some grasses that potentially harm crop development in maize, sugarcane, sorghum, and other crops (Mac Loughlin et al., 2016), and also inhibit some perennial weeds.

Besides, it is used as a non-selective herbicide in railway roads and non-cultured lands. Atrazine products are utilised in formulations of pure atrazine or in ready-to-use combinations with other herbicides applied in pre-emergence or post-emergence (Maceljski et al. 2005). Atrazine is used in 70,000–90,000 tonnes per year across the world (Zhang et al., 2018). Corn for example occupies a special position in the national economy, It is a versatile crop (used for human consumption, animal and poultry feed, and raw materials) (e.g. for starch industry) in Egypt (Galal, 2002; Mohamed, 2020). The competition between weeds and corn is capable of reducing the quality and quantity of corn yield by 33.7% (Saudy, 2013), and about 50% (Abouzinea et al., 2013). Atrazine has high water mobility and ecological tenacity owing to its chemical features and long-term usage as a plant protector; residues

of this herbicide have been discovered in surface, ground, and drinking water samples. and even in animal feed mostly in corns (Gojmerac et al. 1996, Kramer et al. 2001 Waring and Moore, 2004). In spite of being prohibited in the European Union (EU) in 2003 (Bethsass and Colangelo, 2006), atrazine is still in use as a major herbicide in Egypt due to its high efficacy, low price, and its wide-spread among farmers.

ATRZ has received considerable attention as a result of its extensive use and ubiquitous contamination in ground and surface waters, its pattern of use, high persistency, and its potential biological impact in the environment (Hayes et al. 2003). Additionally, atrazine causes inhibition of spermatogenesis, alteration in testicular Sertoli and Leyding cells morphology and decreased accessory sex organ weight; it also lowered epididymal sperm count and motility, and influenced testicular cell morphology (Abarikwu et al. 2010). For a period of 16 days, rat's gavage orally with atrazine there were oxidative changes in the genital area in nature (Adesiyun et al. 2011; Abarikwu et al. 2013). ATRZ also decreases testosterone levels and increases estradiol levels (Victor-Costa et al. 2010). Kniewald et al. (2000) illustrated that atrazine administration may result in reduction of testosterone conversion to 5-dihydrotestosterone (DHT) in the hypothalamus, anterior pituitary, and prostate; decreased pituitary and prostate weights; decreased DHT binding to the androgen receptor; and decreased quantity and motility of spermatozoa. Not only, has it caused alterations in spermatogenesis and a decrease in sperm capacitation, but also it has been hypothesised that it has a negative impact on male rat reproductive function, with a direct effect on the hypothalamic-pituitary-testicular axis (Trentacoste et al. 2001). Furthermore, the sexual system of feral animals may be affected by atrazine (Melachlan et al. 2006). Additionally, adverse effects on the amount of sperm in the testicles and epididymis, motility, viability, morphology, and daily sperm outcome in male rats were observed after oral exposure of atrazine (Abarikwu et al. 2010). ATRZ may behave as an endocrine disruptor, affecting the endocrine system (Rayner et al. 2004). Hepatic damage was reported due to exposure to atrazine in rats (Campos – pereira et al. 2012).

Studies show that atrazine causes adverse effects on the liver, the kidney and cardiovascular system in animals exposed to it (Chan et al. 2007).

Present research has linked oxidative stress (OS) to ATRZ toxicity by examining particular biomarkers in organ's tissues such as the liver, erythrocytes, testis, and epididymis in rats (Singh et al. 2018). ATRZ can potentially have an impact on male reproduction through secondary metabolic consequences. ATZ alters body weight,

promotes oxidative stress, and alters glucose metabolism in immature rats or mice (Lim et al. 2009; Jin et al. 2014, 2015). In both normal and diabetic rats, atrazine treatment resulted in a considerable rise in liver damage indicators such as AST, ALT, and ALP enzymes, as well as kidney damage biomarkers such as creatinine and urea, although this increase was more prominent in diabetic rats (Jestadi et al. 2014). As a close-knit network, the immune system provides a strong protection against the effects of chemical exposure, a study of atrazine's long-term immunotoxicity (Holaskova et al. 2019). Chang et al. (2021) evaluated the toxic effects of different concentrations of atrazine on immune function in mice.

The present study was undertaken to investigate the potential effects of atrazine – induced toxicity in liver, kidney, and tests of male rats through hematological, biochemical, and reproductive biomarkers.

MATERIALS AND METHODS:

Atrazine

- Chemical name: 6-chloro-4-*N*-ethyl-2-*N*-propan-2-yl-1,3,5-triazine-2,4-diamine. (IUPAC).
- Common name: Gesaprime
- Trade name: Atrazine.
- Molecular formula: C₈H₁₄ClN₅
- Used formulation: 80% WP.
- Rate/ Feddan: 0.75 kg/fed.
- This herbicide was supplied from Syngenta Company (USA).
- Toxicity: The oral LD₅₀ of atrazine in rats was determined to be 3000 mg/kg. The oral LD50 for atrazine is 3090 mg/kg in rats. [WSSA, 1994 and U.S. National Library of Medicine, 1995].

Chemicals were of analytical grade purity and obtained from Biodiagnostic Company, 29 Tahreer St., Dokki, Giza, Egypt. **The tested animals and experiments:**

The experiments have been conducted out at Plant Protection Department, Faculty of Agriculture, Damanhour University, El-behera, Egypt.

Animals, Experimental design and sampling:

Healthy Male albino rats (*Rattus norvegicus*) immature stage and weighing 195±5 g, were used in the evaluation of the adverse effects of the sub-lethal doses of atrazine. These rats have been supplied from the National Research Centre's (NRC) Animal Breeding House in Dokki, Cairo, Egypt. Before beginning the studies, the rats were given a week to acclimate. Temperature-controlled settings were used to maintain the rats (25°C). They were provided regular food and allowed

unlimited access to water. Throughout the investigation, clinical evaluations and body weight measurements were performed once a week. The animals were separated into four groups of four rats each, with one group serving as an untreated control.

Dosages of atrazine were freshly prepared and adjusted weekly for body weight changes and given at approximately the same time each morning. Atrazine with the formulated form was administered at a dose 60, 150, and 300 mg a.i kg⁻¹ b.wt. for male rats. Atrazine has oral LD₅₀ of 3090 mg/kg in rats [Weed Science Society of America, 1994 and U.S. National Library of Medicine, 1995]. An equivalent volume of corn oil (0.5 ml /rat) was given to the check (control) group of rats. Rats were split into four groups of four rats each as follows:

The following outlines the experimental groups:

Groups 1: were orally administered doses of formulated atrazine, for 30 days (60 mg a.i /kg b.wt).

Group 2: were orally administered doses of formulated atrazine, for 30 days (150 mg a.i /kg b.wt).

Group 3: were orally administered doses of formulated atrazine, for 30 days (300 mg a.i /kg b.wt).

Group 4: this group served as control (check group) and only acquired a comparable volume of corn oil

Throughout the study, rats were watched for overall behaviour, toxicity signs, and mortality.

Male rats' body weight fluctuations were recorded weekly throughout the study (30 days). Blood was collected from rats 24 hrs, after the end of 30 days, via heparin-treated tubes and non-heparin-treated tubes for the analysis of plasma and serum, respectively. Blood was kept at room temperature for 20 minutes before being centrifuged for 10 minutes at 3000 rpm (600g) using a Hereaus Labofuge 400R, Kendro Laboratory Products GmbH, Germany, to separate the serum as well as plasma, respectively. Rats were slaughtered by decapitation after 24 hours after the last treatment at the end of the experiment. Male rats' organs were swiftly removed, cleaned, and weighted separately. The organ/body weight ratios were then computed.

Biochemical parameters:

Haematological and biochemical parameters were determined as follows:

- 1- Serum alkaline phosphatase (ALP/AP) according to the method described by **Rec (1972)**.
- 2- Serum acid phosphate measurement was carried out according to the method described by **Belfield (1971)**.

- 3- Serum aspartate amino transferase (AST, EC.2.6.1.1) and Serum alanine amino transferase, ALT (EC.2.6.1.1) according to the method described by **Reitman and Frankel (1957)**.
- 4- Serum blood glucose levels were measured using the technique outlined by **Trinder (1969)**
- 5- Total protein content calculated using the technique outlined by **Young (2001)**.
- 6- Total cholesterol in the serum was estimated using the approach outlined by **Trinder (1969)**.
- 7- Serum uric acid measurement was conducted by using the procedure outlined by **Fossati et al., (1980)**
- 8- Serum creatinine concentration was determined using the protocol of **Henry (1974)**.
- 9- Testosterone determination in conformity with the provisions given by (**Turkes (1979)**). Testes as well as epididymis of four male rats from each subgroup were processed for sperm analysis (**Lubicz-Naworcki and Chang, 1974**). Number of sperm was counted, and the motility of epididymal sperm was assessed as a proportion that became increasingly motile
- 10- Triiodothyronine (T₃) Hormone assessment was conducted out using the procedure described by (**Cavaliere and Rapoport, 1977**) using International Immuno Diagnostics Kits.
- 11- Thyroxine (T₄) Hormone analysis was conducted via the method estimated by (**Schuurs and Van Weeman, 1977**) using International Immuno Diagnostics Kits.
- 12- The crude homogenates of the tests, liver, and kidney were prepared according to Ohkawa et al., (1979).

Statistical analysis:

The acquired data was statistically analysed in accordance with Snedecor and Cochran (1967), and the least significant differences (LSD) at the 5% level of significance were computed. The statistical analysis system (SAS) version 9.2 (SAS, 2013) computer programme was used to examine all data.

RESULTS AND DISCUSSION:

It is important from the safety point of view which is correlated directly to human health to evaluate the detrimental side effects of herbicides on mammals by using male albino rats as an experimental animals model. Formulations of pesticides are complex combinations, and toxicity data on active components alone are insufficient to assess the likelihood of adverse health consequences from commercial pesticides. Thus,

the purpose of this study was to see how subacute administration to formulated atrazine affected haematological, biochemical, and hormonal markers in the blood of treated rats.

Doses of 60, 150, and 300 mg a.i./kg/day are taken orally every day to male rats for 30 days. There were no obvious indicators of toxicity or death in the treated rats throughout the period of investigation.

2- Effects of atrazine on blood plasma and liver homogenates biochemical parameters:

Estimating the activity of enzymes found in serum is useful tool to disorder assessment. This pick any disturbances to the system early enough to allow for projection and possible remedies. In the light of this, selected serum enzymes and biochemical parameters were assayed in the serum of rats given daily oral sub-lethal doses of atrazine for 30 days. Results in Table (1) show that atrazine with the highest two tested doses (150 and 300 mg a.i./kg b.w.) increased significantly the activity of the serum acid phosphatase (ACP), serum alkaline phosphatase (ALP), serum aspartate transferase (AST), serum alanine amino transferase (ALT), and total cholesterol. Atrazine at all tested doses significantly decreased the concentration of total protein and glucose in comparing with those in the untreated treatment. The highest doses of atrazine (150 and 300 mg a.i./kg b.w.) elevated the activity of ACP from 4.19 U/l in control to 5.39 and 6.08 U/l, respectively. Furthermore, these doses increased the activity of ALP from 98.45 U/l in control to 118.92 and 131.64 U/l, respectively. Also, these doses increased the activity of AST from 35.46 U/ml in control to 43.39 and 47.98 U/ml, respectively, and shift the activity of ALT from 38.72 U/ml to 50.41 and 60.02 U/ml, respectively, in serum of atrazine.-treated rats.

On the other hand, all tested doses of atrazine (60, 150 and 300 mg a.i./kg b.w.) caused significant decrease in glucose content from 50.58 mg/dl in control to 42.39, 37.48 and 29.85 mg/dl, respectively, and decreased total protein from 6.69 g/dl in control to 5.37, 4.59 and 3.78 mg/dl, respectively, in a dose- dependent response. However, total cholesterol content was elevated from 56.53 mg/dl in control to 89.70 mg/dl, with the dose (300 mg a.i./kg b.w.) of atrazine as illustrated in table (2).

The lowest tested dose of atrazine (60 mg a.i./kgb.w./day) did not affect significantly ALP, AST, and ALT levels in the serum of treated-rats.

Liver is frequently the first target of ingested substances before they enter the bodily fluids; therefore, it is subjected to high quantities of these chemicals [Irving and Elfarra, 2012].

ALT is thought to be more specific for hepatic injury because it is present mainly in the cytosol of the liver and in low concentrations elsewhere [Campos-Pereira et al. 2012]. The elevation of ALT in the current study was attributed specifically to the injury of liver cells caused by atrazine [Konstantinova and Russanov, 1999], whereas the AST is a mitochondrial enzyme found in the heart, liver, skeletal muscle, and kidney and is normally present in plasma [Fowler et al. 2012]. Serum AST rise is appears to be the result of mitochondrial damage caused by reactive oxygen species (ROS) generated by atrazine [Zilva et al. 1988].

Jestadi et al. (2014) stated as follows short term exposure of atrazine at $300\mu\text{g kg}^{-1}$ potentially because oxidative stress in liver, led to significant increase in biomarkers of liver injury, such as AST and ALT, as well as ALP, this rise was observed in both normal and diabetic rats, although it was more prominent in diabetic rats than in normal rats. Atrazine's harmful effects may be due to the production of reactive oxygen species (ROS), which causes oxidative stress in numerous tissues. Herbicide-induced hepatic damage is thought to be caused by increased oxidative stress and lipid peroxidation [Mohammad, et al. 2012]. Rat liver damage might be caused by atrazine [Adesiyan et al. 2011]. Higher ALT and AST levels in atrazine treated-animals might be caused to aminotransferase enzyme leaking from damaged liver cells (Konstantinova and Russanov, 1999, Jestadi et al. 2014). A raise in enzymatic levels of ALT and AST in extracellular fluid or plasma may be a useful indicator of cellular liver damage or pathological alterations such as apoptosis of hepatocytes trigger an increase in cell membrane permeability, leading in aminotransferase release via the blood circulation [Ali et al. 2008]. Regarding the reduction of total protein content in our study, Yousef et al. (2006) stated that a reduction in plasma proteins might be due in part to pesticides' reversal action on liver cells. Moreover, reduction in plasma protein might occur because of physiological adaptation of animals to combat stress produced by pesticide. In various in vivo and in vitro model systems, atrazine causes oxidative damage, cytotoxicity, and apoptosis [Adesiyan et al., 2011, Abarikwu et al., 2015, Campos-Pereira et al., 2012], hepatotoxic effects [Gojmerac et al., 1995, Abarikwu, 2014, Singh et al., 2011].

However, rats treated with 400 mg kg^{-1} atrazine for 14 consecutive days resulted in nonsignificant elevation in serum ALT enzyme [Hussain et al., 2012].

Table (1): Acid phosphatase, alkaline phosphatase, AST, and ALT activities alterations in the serum of rats in rats administered 30 repetitive oral doses of atrazine.

Treatments	Dose	Acid phosphatase (U/l)		Alkaline Phosphatase (U/l)		AST (U/ml)		ALT (U/ml)	
	mg a.i./kg b.w.	Activity (U/l)	% of control	Activity (U/l)	% of control	Activity (U/ml)	% of control	Activity (U/ml)	% of control
Control	0.00	4.19 ±0.03895 ^d	100.00	98.45 ±4.303690 ^c	100.00	35.46 ±0.251054 ^c	100.00	38.72 ±2.070553 ^c	100.00
Atrazine (Formulation form)	60	4.73 ±0.00704 ^c	112.89	102.91 ±5.27698 ^c	104.53	38.68 ±3.884268 ^{bc}	109.08	44.9 ±2.605792 ^{bc}	115.95
Atrazine (Formulation form)	150	5.39 ±0.03895 ^b	128.64	118.92 ±4.850997 ^b	120.80	43.39 ±2.05894494 ^{ab}	122.36	50.41 ±3.628609 ^b	130.20
Atrazine (Formulation form)	300	6.08 ±0.014605 ^a	145.11	131.64 ±8.323697 ^a	133.71	47.98 ±3.921770 ^a	135.31	60.02 ±3.626866 ^a	155.01

Each value is a mean ± SD; Statistical difference from the control: Means in the same columns with the same letter are not significantly different.

2- Effects on blood plasma and kidney homogenates biomarkers:

Creatinine and uric acid in the serum of animals seem to be beneficial in the early detection of foreign compound-induced nephrotoxicity. Results in Table (2) revealed that Creatinine (mg/dl) and uric acid (mg/dl) concentrations were considerably raised in the serum of atrazine-treated rats in a dose-dependent approach, relative to control. Thus, the dose of (300 mg a.i./kg b.w.) of atrazine caused a considerable increase in creatinine from 0.5982 mg/dl in un-treated rats to 0.8962 mg/dl, and in uric acid concentration from 4.2756 mg/dl in un-treated rats to 6.787 mg/dl. Atrazine with the lowest dose did not affect

creatinine concentration significantly in comparing with the untreated treatment. The change in creatinine and uric acid concentrations in the blood of treated rats might be related to a decrease in glomerular filtration in the kidney, as well as malfunction of the kidney tubules. (Walmsley and white, 1994).

Liu et al., (2014) reported that for 28 days, Females Wister rats were given 0, 5, 25, and 125 mg/kg atrazine, and their serum levels of creatinine and uric acid increased. In several in vitro and in vivo model systems, atrazine causes nephrotoxicity [Jestadi et al., 2014, Liu et al., 2014]

Table (2): Effect of atrazine on the concentration of Glucose, Total Protein, Total Cholesterol, Creatinine and Uric acid in the serum of male rats administered daily oral doses for 30 days.

Treatments	Dose	Glucose		Total protein		Total Cholesterol		Creatinine		Uric acid	
	mg a.i./kg b.w.	Conc. (mg/dl)	% of control	Conc. (g/dl)	% of control	Conc. (mg/dl)	% of control	Conc. (mg/dl)	% of control	Conc. (mg/dl)	% of control
Control	0.00	50.58±3.367580 ^a	100.00	6.69±0.190196 ^a	100.00	56.53±2.502766 ^d	100.00	0.5982±0.041141 ^c	100.00	4.2756±0.073269 ^d	100.00
Atrazine (Formulation form)	60	42.39±1.860562 ^b	83.81	5.37±0.165433 ^b	80.27	66.76±4.599385 ^c	118.10	0.6803±0.043204 ^{bc}	113.72	5.237±0.233913 ^c	122.49
Atrazine (Formulation form)	150	37.48±3.799429 ^b	74.10	4.59±0.147426 ^c	68.60987	74.96±3.116789 ^b	132.60	0.7663±0.041177 ^b	128.10	5.929±0.282929 ^b	138.67
Atrazine (Formulation form)	300	29.85±3.957022 ^c	59.02	3.78±0.159912 ^d	56.50	89.70±4.758613 ^a	158.68	0.8962±0.042014 ^a	149.82	6.787±0.076818 ^a	158.74

Each value is a mean ± SD; Statistical difference from the control: Means in the same columns with the same letter are not significantly different.

3- Effects of different treatments on T₃ (ng/dl), T₄ (µg/dl), Testosterone (ng/ml), sperm account (NX10⁶/ml), sperm motility (%) in blood plasma and tests homogenates

Results in Fig. (1) revealed that at the end of administration period (30 days) of sub-lethal doses of atrazine to male rats caused a considerable increase in T₃ levels were in a dose-dependent pattern. While the highest tested dose (300 mg a.i./kg b.w.) only resulted in a considerable increase of T₄ hormone in the serum of rats that had been treated. In case of testosterone hormone, all tested doses of atrazine caused significant decrease in the serum of rats that had been treated, in a dose-dependent response, relative to control, the same trend observed in case of sperm account/ml and sperm motility. The highest dose of atrazine (300 mg a.i./kg b.w.) caused a significant increase in T₃ from 128.55 ng/dl in control to 183.82 ng/dl, and increased T₄ concentration from 9.175 µg/dl in control to 9.891 µg/dl, in the serum of rats that had been treated. While, the highest dose of atrazine caused significant decrease in testosterone concentration from 2.61785 ng/dl in control to 1.02955 ng/dl in the serum of rats that had been treated, and resulted in considerable decrease in sperm account/ml from 63.62x10⁶/ml in control to 42.61x10⁶/ml in the serum of treated rats. Sperm motility was significantly decreased from 91.75% in control to 70.25% in the serum of rats that had been treated with the highest dose of atrazine (300 mg a.i./kg b.w.). Pesticides may disrupt thyroid function by interfering with the hypothalamic pituitary thyroid (HPT) axis, inhibiting iodine intake by the thyroid gland, increasing excretion of thyroid hormones, decreasing cellular uptake of thyroid hormones, and changing the expression of thyroid hormone-regulated genes. [Goldner et al., 2013].

These hormonal alterations were in agreement with several studies, that atrazine can operate as an endocrine disruptive chemical with endocrine system impacts [Hayes et al. 2003, Rayner et al. 2004, Spano et al. 2004].

Statistical analysis of our results in Fig. (1) revealed a considerable decrease changes the levels of testosterone hormone in herbicide-treated rats' serum. The considerable fall in testosterone levels (ng/ml) may be due to atrazine's direct damage to leydig cells, which are the primary location of testicular androgen production. Testosterone is essential for sex organ development and sperm production (Robinson and Huntale, 1988), that atrazine has the potential to cause harm in the reproductive system of rats and animals in the wild [McLachlan et al., 2006, Adesiyani et al., 2011]

Daradkeh et al. (2020) reported that wistar rats orally administered by different doses of the herbicide atrazine; (27.3, 38.5, and 42.0 mg

kg⁻¹ b.w), elevated concentrations ($p \leq 0.05$) of thyroid stimulating hormone (TSH) compared to control were observed through the course of the experiment. Increasing moles of other sprayed herbicides was found to increase T₄, while others elevated levels of TSH.

The impact of atrazine on the thyroid gland revealed a substantial rise in blood T₃ levels in male rats given 200 mg/kg body weight (bw) [Stoker et al. 2000]. A previous study illustrated that serum T₃ concentration was considerably elevated at 200 mg/kg bw per day, indicating that atrazine can postpone the beginning of puberty and change estrous cyclicity in the female Wistar rat. The method of action appears to involve changing steroid production, most likely as a result of central nervous system disturbance of pituitary function regulation.

Friedmann (2002) reported that in vivo experiments serum and intratesticular testosterone levels were lowered by roughly 50% in both acute and chronically atrazine treated animals. The findings show that atrazine works as an endocrine disruptor in rat males by directly suppressing testosterone synthesis in Leydig cells.

Atrazine dosing of up to 50 mg/kg per day had no influence on any of the examined variables, according to the study. Atrazine lowered serum testosterone concentrations by 100 and 200 mg/kg per day, as did seminal vesicle and ventral prostate weights. Even minor food restriction led in decreases in blood testosterone concentration, weights of androgen-dependent organs, and serum LH concentration, the same deficiencies reported in atrazine-gavage rats. Indeed, the effects of atrazine on the male reproductive system in rats given more than 50 mg/kg per day could not be separated from the effects of lower food consumption. These findings indicate that caution should be maintained before assuming that atrazine (or any potentially harmful substance) has direct and negative consequences (Trentacoste et al., 2001). Gonadotropin suppression (necessary for proper sperm production) qualifies for reducing density of sperm in cauda epididymis and the testes. Changes in androgen metabolism may contribute to low caudal epididymal sperm density (Choudhary et al., 2008).

Joshi et al. (2012) cited that administration of herbicides such as butachlor were administered to male rats, led to a substantial reduction in sperm capacitation and density. The sharp reduction of sperm motility may be due to a low amount of adenosine triphosphate (ATP) (Bai and Shi, 2002). Alterations in the enzymatic activity of the oxidative phosphorylation process, which is essential for the synthesis of ATP, a source of energy for the forward movement of spermatozoa, may have an effect on sperm motility (Joshi et al. 2007). In addition, Exposure to

pesticides has been linked to altered thyroid function as well as lower testosterone and

oestrogen levels, potentially contributing to infertility later in life. (Gilden et al., 2010).

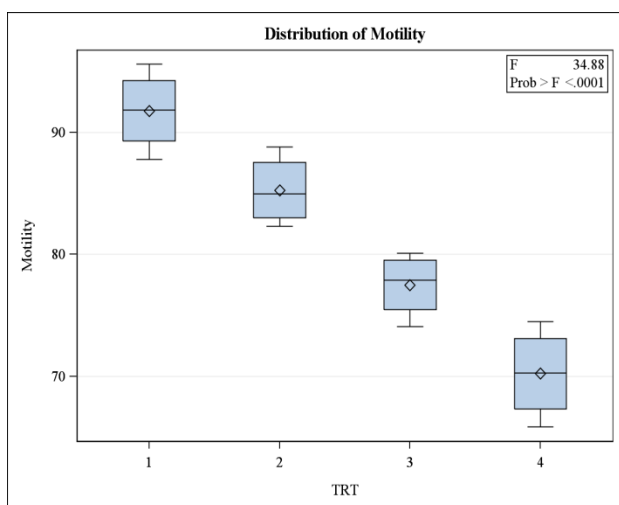
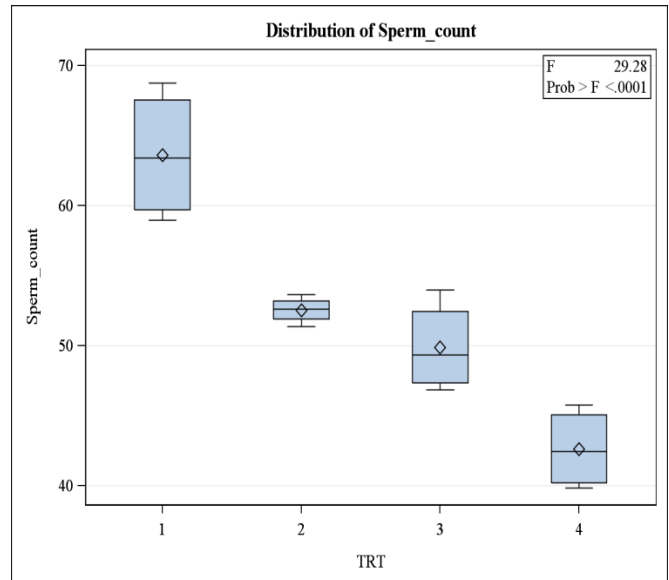
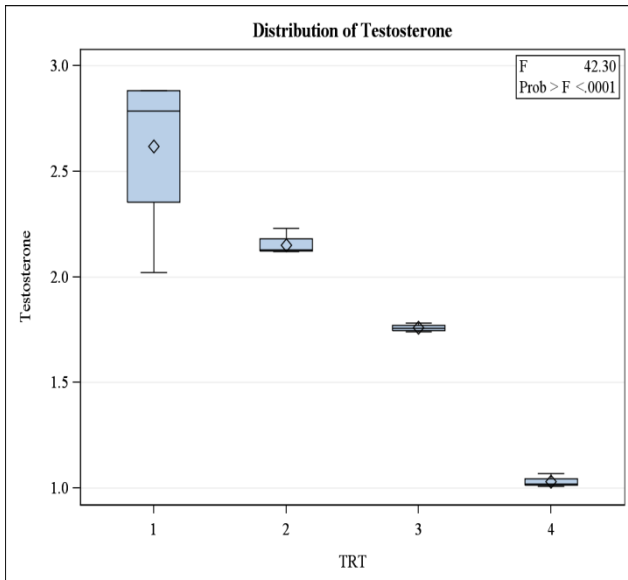
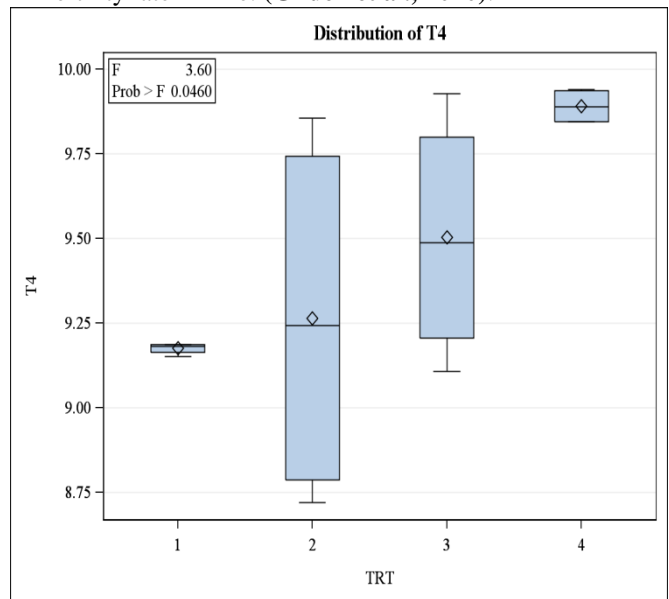
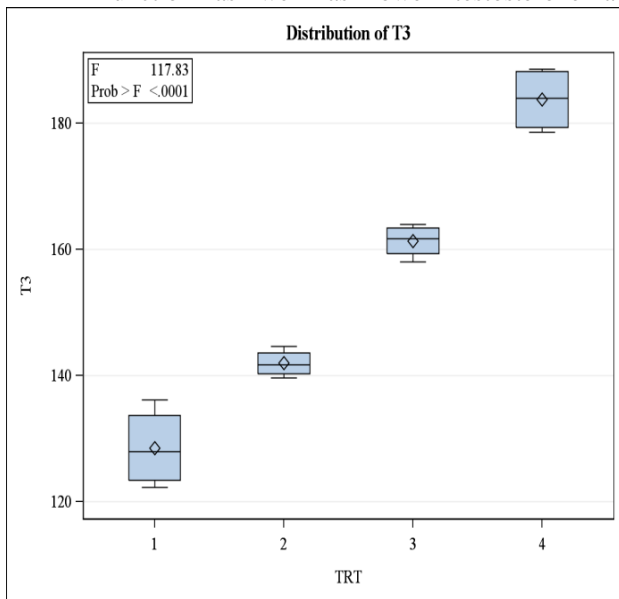


Fig. (1): The influence of the tested doses of atrazine on the levels of T3, T4, Testosterone hormones, and sperm account & motility in the serum of male rats given daily oral doses for 30 days.

- 1- Control.
- 2- Atrazine (Formulation form) (60 mg/kg b.w).
- 3- Atrazine (Formulation form) (150 mg/kg b.w).
- 4- Atrazine (Formulation form) (300 mg/kg b.w).

4- Effect of tested herbicides on body and organs weights

After dosing period, data in Table (3) clarify that treatment of rats with the tested doses of atrazine achieved considerable body weight reduction relative to control in a dose-dependent response. The highest dose atrazine caused significant reduction in rats weight gain from 239.08 g in control to 195.25 g. Also results in table (3) revealed that the testes absolute and relative weights (g) were markedly decreased, while Because of the exposure, the relative weights of the liver and kidney increased significantly. The absolute weight of liver was increased with atrazine highest tested doses. However, absolute kidney weight in herbicide-treated rats considerably less than that of the control without any significant changes between them, while all tested doses of atrazine resulted in a dose-dependent response, there was a considerable rise in the absolute and relative weights of splin.

Organ and relative organ weights are significant factors for evaluating organ toxicity in toxicological research. (Crissman et al. (2004)). Exposure to agricultural chemicals frequently results in a loss of body weight and organ weights in animals [Dutta and Sahu, 2013]. Atrazine administration resulted in either unchanged or lowered body weights [Kandori et al. 2005, Mossa et al. 2013]. Body weight and organ weight decline (i.e., liver and kidney) following atrazine medication might be attributed to a lower calorie intake or necrotic alterations in various body tissues. [Fukamachi et al., 2004].

Trentacoste et al. (2001) stated that the reduction body weight average of atrazine treated rats at 100 mg/kg per day was about 9%. This showed that the effects of atrazine on the reproductive system may not be direct, but rather that the observed impairments in the male reproductive tract arose from the treated rats' lower food intake.

Current researches have linked oxidative stress to ATRZ toxicity by examining particular biomarkers in organs such as the rat's liver, erythrocytes, testis, and epididymis. [Abarikwu et al., 2010, Adesiyan et al., 2011, and Singh et al., 2011]. ATRZ induces suppressive effects on gonadal endocrine system's function in both male and female (Kretser and Kerr, 1995, Kniewald et al. 1995).

Feyzi-Dehkhargani et al. (2012) stated that ATRZ had a negative effect on the endocrine function of the testes and pituitary gland, and also had an influence on the cytoplasmic CH ratio, which leads to insufficient energy supplementation in spermatogenesis cells. As a result, testicular tissue experiences unbalanced oxidative stress, which increases sperm DNA disintegration and nuclear immaturity. Furthermore, it alters morphology of sperms and decreases its motility (Kniewald et al., (2000).

Mokhtari et al. (2010) stated that a considerable decrease in mean body weight in experimental groups compared to control groups. Only the experimental groups that received 200,400 (mg/kg) of atrazine had a reduction in testes weight.

Table (3): Body and organs weights changes in rats administered 30 repetitive oral doses of atrazine.

Treatments	Dose mg a.i./kg b.w.	Initial weight (gm)	Final weight (gm)	% Change	liver weight (gm)	Kidney weight (gm)	spleen weight (gm)	Lung weight (gm)
Control	0.00	192.75 ±5.200321 ^a	239.08 ±4.018603 ^a	100.00	4.11 ±0.065828 ^c	1.9929 ±0.052333 ^a	0.620 ±0.006378 ^d	1.2028 ±0.012685 ^c
Atrazine (Formulation form)	60	193.20 ±3.831449 ^a	228.72 ±4.636903 ^b	76.67	4.08 ±0.052915 ^c	1.9170 ±0.039246 ^a	0.680 ±0.020801 ^c	1.2260 ±0.004690 ^c
Atrazine (Formulation form)	150	199.50 ±4.633213 ^a	220.48 ±4.106093 ^b	45.28	4.36 ±0.073937 ^b	1.9210 ±0.012353 ^a	0.820 ±0.010801 ^b	1.6750 ±0.003742 ^b
Atrazine (Formulation form)	300	198.79 ±1.9629223 ^a	195.25 ±5.776101 ^c	-7.64	4.68 ±0.112842 ^a	1.93230 ±0.054491 ^a	0.906 ±0.041481 ^a	1.9960 ±0.054565 ^a
Treatments	Heart weight (gm)	Testis weight (gm)	Relative liver weight	Relative kidney weight	Relative spleen weight	Relative lung weight	Relative heart weight	Relative testis weight
Control	0.6545 ±0.003862 ^c	4.1176 ±0.008099 ^a	0.01719 ±0.00042 ^c	0.00834 ±0.00021 ^c	0.00259 ±0.000064 ^d	0.00503 ±0.0000896 ^d	0.00274 ±0.0000332 ^d	0.01722 ±0.0003211 ^a
Atrazine (Formulation form)	0.6590 ±0.016269 ^c	3.9260 ±0.073050 ^b	0.01784 ±0.00055 ^c	0.00838 ±0.00017 ^{bc}	0.00297 ±0.000134 ^c	0.00536 ±0.0001239 ^c	0.00288 ±0.0000330 ^c	0.01717 ±0.0005081 ^a
Atrazine (Formulation form)	0.7289 ±0.003862 ^b	3.5076 ±0.089340 ^c	0.01978 ±0.00021 ^b	0.00871 ±0.00022 ^b	0.00372 ±0.00011 ^b	0.00760 ±0.0001539 ^b	0.00331 ±0.0000562 ^b	0.01591 ±0.0003201 ^b
Atrazine (Formulation form)	0.8519 ±0.004899 ^a	2.9245 ±0.013916 ^d	0.02397 ±0.00021 ^a	0.00990 ±0.00011 ^a	0.00464 ±0.000219 ^a	0.01022 ±0.0001379 ^a	0.00436 ±0.0001076 ^a	0.01498 ±0.0004989 ^c

Each value is a mean

± SD; Statistical difference from the control: Means in the same columns with the same letter are not significantly different.

CONCLUSION:

In conclusion, atrazine is toxic to the body, blood, kidney, and liver functions of exposed rats and may have long-term severe effects on human health and the environment. This strongly indicates that proper precautions need to be taken in use of pesticides; there are further studies needed for the better understand the toxicity and safety references of herbicide formulations produced and applied in Egypt.

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الملخص العربي

التأثيرات البيوكيميائية للمعاملات بمبيد الأترازين في ذكور الجرذان البيضاء

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قد يشكل الثبات البيئي والتراكم الأحيائي لمبيد الحشائش الأترازين الذي يتبع مجموعة كلورو ترايأزينات المتماثلة مصدر قلق كبير لصحة الإنسان. في هذه الدراسة، أعطيت جرزان التجارب البيضاء باوزان 5 ± 195 جرام، عن طريق الفم جرعات 0، 60، 150، و 300 ملغ مادة فعالة / كجم من وزن الجسم أترازين، على التوالي، يوميا لمدة 30 يوما. تم تم تقييم و تحليل وظائف الكبد والكلى و اضطرابات الغدد الصماء و حساب الحيوانات المنوية و حركة الحيوانات المنوية وأوزان أعضاء الجسم (المطلقة و النسبية). خلال فترة الدراسة ، لوحظت الفئران للسلوك العام وأعراض السمية والوفيات. في نهاية الدراسة، تم تشريح الجرذان بعد 24 ساعة، من المعاملة الأخيرة . الكبد، الكلى، الرئتين، القلب، الطحال ، والخصيتين في ذكور الجرذان تم إزالتها بسرعة غسلها ووزنها بشكل فردي. ثم تم حساب الوزن النسبي للأعضاء المأخوذة و ذلك بخارج قسمة وزن العضو إلى وزن الجسم، وتم جمع الدم من الفئران 24 ساعة، بعد نهاية الـ30 يوما (زمن التجربة) . لم يسبب الأترازين مع الجرعات المختبرة أي علامات واضحة على سمية أو وفيات الفئران المعاملة طوال فترة التجربة (30 يوما). و أوضحت النتائج أن معاملة ذكور فئران التجارب البيضاء بالجرعات المختبرة من الأترازين حدوث خفض في زيادة وزن الجسم، و حدوث خفض في الحيوانات المنوية، في حين تم حدوث زيادة في أوزان الأعضاء (باستثناء الخصيتين تم تخفيضه، في حين لم يؤثر على الوزن المطلق للكلى)، وتم حدوث زيادة في نشاط انزيمات الكبد و انزيمات الكلى محل الدراسة (باستثناء البروتين والجلوكوز و التي انخفضت قيمها معنويا) و كذا تم حدوث زيادة معنوية في تراكيز هرمون T3 بصورة تعتمد على الجرعة في حين تم زيادة تراكيز هرمون T4 فقط مع أعلى جرعة مختبرة من الأترازين في الفئران المعاملة مقارنة بتلك الغير معاملة بمعاملة الكنترول. وبمعنى اخر، فإن الأترازين يعتبر سام لوظائف الجسم والدم والكبد والكلى للفئران المعرضة و كذا كمادة كيميائية مؤثرة على الغدد الصماء و التي قد تكون لها آثارا ضارة على صحة الإنسان والبيئة المحيطة به بعد التعرض له لفترة طويلة..