


## ATRAZINE AS AN ENDOCRINE DISRUPTOR AND ITS EFFECTS ON MALE REPRODUCTIVE HEALTH

 <https://doi.org/10.56238/arev6n2-099>

Date of submission: 10/09/2024

Date of publication: 10/10/2024

**Aniely Loiza Pedrozo<sup>1</sup>, Humberto Manabu Oda<sup>2</sup>, Nasle Dogan<sup>3</sup>, Weslen Fernandes da Silva Matusiaki<sup>4</sup> and Miriam Hiroko Inoue<sup>5</sup>**

### ABSTRACT

Atrazine has been widely used in Brazilian agriculture, especially in corn and soybean crops. Due to its widespread use, this literature review is relevant to systematize the main studies that evaluate the impact of atrazine as an endocrine disruptor leading to changes in fertility quality, especially in males. In several tests and studies carried out with the exposure of animals to atrazine, negative effects related to changes in factors that are essential for male fertility were observed. Therefore, inhibition of the hypothalamic-pituitary-testicular axis, decreased reproductive cells's metabolic activity, reduced testosterone levels, reduced lactate dehydrogenase (LDH) enzyme, negative effects on spermatogenesis and morphological changes in the gonads and sperm are results of atrazine toxicity on the male reproductive system that contribute to infertility. In general, it is concluded that atrazine has a potential endocrine disruptor effect, leading to changes in the form of hormone production, especially in hormones related to male sexual reproduction. For this reason, assessing the risks of exposure to this toxin at different stages of life and over several generations, combined with knowledge of its pathophysiological mechanism on the male reproductive system, is essential to preserve the reproductive health of future generations.

**Keywords:** Atrazine. Endocrine Disruptor. Male Infertility.

---

<sup>1</sup> Pharmacist specializing in Facial and Body Aesthetics  
Faculty of Applied Social Sciences

<sup>2</sup> Graduated in Law, studying for a master's degree in Environment and Agricultural Production Systems  
Mato Grosso State University

<sup>3</sup> Law graduate Master's student in Environment and Agricultural Production Systems  
Mato Grosso State University

<sup>4</sup> Graduated in Chemistry, studying for a master's degree in Environment and Agricultural Production Systems  
Mato Grosso State University

<sup>5</sup> Doctorate in Agronomy  
Mato Grosso State University

## INTRODUCTION

Progress in agricultural development and population growth are intrinsically linked. According to projections by the Food and Agriculture Organization (FAO), by 2050 the world population will exceed 9.5 billion people, so requiring a substantial increase in the food supply. However, in 2023, the FAO classified 733 million people as suffering from food vulnerability. This raises concerns for the future since, in addition to population increase, there is likely to be increased per capita consumption and per capita income, climate change, as well as restrictions to the expansion of the agricultural frontier and continuing increase in cities. Together, these may result in the inability of agriculture to meet future food demands (FAO, 2024).

Accordingly, and with the aim of increasing agricultural production, the use of herbicides to control weeds is a common practice. And, due to their increasing deployment, studies evaluating the impact of these agricultural inputs on human health have also grown (Centanni, *et al.*, 2023; Mohammed *et al.*, 2023; Zhao *et al.*, 2024; Gomes-Andrade *et al.*, 2024).

Among the widely used herbicides, atrazine (IUPAC name: 6-Chloro-N<sup>2</sup>ethyl-N<sup>4</sup>(propan-2-yl)-1,3,5-triazine-2,4-diamine) a compound from the class of triazines, is considered to be one of the most commonly used on corn and sugar cane crops. However, this massive consumption has largely overlooked the broad toxicity of this compound to both the environment and living organisms (Vizioli *et al.*, 2023; Chang *et al.*, 2022).

Considered a persistent pollutant due to its low absorption characteristics, long half-life in soils and moderate solubility, atrazine is commonly found as a contaminant of surface or groundwater and in agricultural soils (Vizioli *et al.*, 2023; Puvvula *et al.*, 2021). As a result, a number of pathways exist by which atrazine and its metabolites can be absorbed by living organisms. These include ingestion, inhalation and direct contact. Accordingly, due to the risks posed to health and the ecosystem, Atrazine was banned in the European Union in 2004 due to the extensive contamination of water (Sass & Colangelo, 2006).

Even though pesticides have greatly increased the quantity of food produced, there are studies that question the real need for their use. Numerous authors advocate organic farming to maintain the health of the soil, people and ecosystems, rejecting the use of pesticides and methods they consider to be environmentally harmful (Javier, 2022; Brito *et al.*, 2023; Martínez-Alfaro & Zuñiga-Orozco, 2024).

However, despite the growing interest in sustainable and organic agriculture, the growth in the use of pesticides in arable fields remains widespread, especially for herbicides, which are continuing to be widely used in countries with large agricultural frontiers, such as Brazil and the United States (EPA, 2020; Chang *et al.*, 2022).

Thus, human exposure to pesticides in their occupational or natural environment has been reported widely in the scientific literature and, following the growth of this exposure, the occurrence of exposure-related diseases has begun to manifest. As a result, there is now considerable scientific interest in the possible relationships between contact with these environmental contaminants and the emergence of a gamut of pathologies (Centanni *et al.*, 2023; Puvvula *et al.*, 2021; Ge *et al.*, 2021).

A growing number of studies have sought to evaluate atrazine toxicity to organic systems, with the impacts it may have on fertility being one of the most studied (Gomes-Andrade *et al.*, 2024; Rotimi & Adeyemi, 2023; Rotimi, Ojo & Adeyemi, 2024; Rodríguez-Robledo *et al.*, 2022). The association with infertility is mainly due to the action of atrazine as an endocrine disruptor (Rotimi & Adeyemi, 2023; Gomes-Andrade *et al.*, 2024; Zhao *et al.*, 2024). Research using animal models has shown that atrazine inhibits the function of the hypothalamic-pituitary-testicular axis (Rotimi, Ojo & Adeyemi, 2024), causing testicular atrophy and degeneration, thus impairing spermatogenesis (Govers *et al.*, 2019; Abarikwu *et al.*, 2024a, Pandey *et al.* 2021), so reducing sperm concentration and motility (Hassanin *et al.*, 2024; Leet *et al.*, 2022, Pandey *et al.* 2021), and resulting in gonadal inflammation (Abarikwu *et al.*, 2024b), and oxidative stress (Mohammed *et al.*, 2023). There has been warning of the risks of chronic exposure (Galoppo *et al.*, 2020), as well as accumulation of metabolites in seminal plasma (Rodríguez-Robledo *et al.*, 2022), which can produce transgenerational effects that may impair fertility in subsequent generations (Thorson *et al.*, 2020; Tan *et al.*, 2021). This current review addresses the effects of atrazine as an endocrine disruptor and its effects on the male reproductive system.

## **MATERIAL AND METHODS**

A qualitative bibliographic review was developed using an analytical interpretation of the studied phenomenon. Such a qualitative perspective underpins the broad, and integrated, approach to the study topic and the correlation of various factors and events with analysis and perception of the internal dynamics of the processes involved.

This type of scientific product also contributes to the development of critical internal and external analysis and, consequently, drives scientific dissemination from both a theoretical and methodological standpoint (Botelho 2011; Lakatos & Marconi, 2003).

To obtain relevant studies, a comprehensive search for articles between 2020 and 2024 was carried out in Scopus with the title filter "atrazine", to find studies that had conducted research with this pesticide. For the keywords, the following filters were used: "fertility", "infertility", "reproduction", "sperm" and "endocrine".

Studies selected were chosen according to the following criteria, that the paper:

- Was an original article (review articles, conference abstracts, editorials and book chapters were excluded);
- Concerned Atrazine exposure;
- Dealt with male reproduction.

Finally, the selected articles were analyzed, and a database was constructed containing the relevant information from each article. This was then used to produce the content presented here.

## RESULTS

The Scopus search returned 75 records. Of these, 16 articles were selected as fully meeting the selection and filtering criteria, the other 51 were excluded.

The studies were selected and organized as the Table 1: Table 1

Concentration	Population Study	Duration	Effects	Study
50 mg/kg	Mices	3 days	↓ Body Weight in the testis = Estradiol and DHT concentration in the testis ↓ Seminal vesicle	Abarikwu et al. (2024a)
			weight = Epididymis eight ↑ Estradiol concentration in the epididymis ↓ DHT concentration in the epididymis	

25mg/kg	Mices	30 days	<p>Absolute testis weight was not affected</p> <p>↓ TNF-<math>\alpha</math> in the testis</p> <p>↑ IL-6 level</p> <p>↓ nitric oxid concentration</p> <p>↓ myeloperoxidase activity</p> <p>Dead cells in the epithelium of the tetis</p> <p>Seminiferous tubules degenerated</p> <p>Desquamates germ cells mostly round spermatids in the lumen</p> <p>Few inflammatory cells in the interstitial areas</p>	Abarikwu et al. (2024b)
0.3, 3, 30, 300, 3000 $\mu$ g/L	Mouse Sertoli cellline	24 hours	<p>↓ Metabolic activity = Mitochondrial function and reactive oxygen species production</p> <p>↓ Lactate dehydrogenase expression in mouse Sertoli cells</p>	Gomes-Andrade et al. (2024)
50 mg/kg bw of atrazine 20 mg/kg body weight of resveratrol	Male albino rats	2 months	<p>↓ Ability of male rats to fertilize</p> <p>↓ Serum level of testosterone hormone</p>	Hassanin et al. (2024)
20 $\mu$ M, 100 $\mu$ M, 250 $\mu$ M of atrazine 20 $\mu$ M, 100 $\mu$ M, 200 $\mu$ M of Diaminochlorotriazine	Egg-laying quail	144 hours	<p>↓ Reduced the Viability of Granulosa Cells (GCs)</p> <p>↑ Steroid Hormone Disruption in GCs</p> <p>↑ Apoptosis in GCs</p>	Xiao-Wei et al. (2024)
0.7, 7.0, 70 $\mu$ g/L ATZ	O. bonariensis larvae	4 weeks	↑ Testicular germ cell number	Carririborde et al. (2023)
Exporure to environmental pollutants where the mother was living when the clid was born	Samples from newborn	Birth between January 1, 2021 and December 31, 2021	No significant tap-water contamination associated with TSH concentration	Chamot et al. (2023)

0.02 ng/mL	Mices	3 weeks	No effect on litter size, litter weight, sex ratio or mortality rates or across generations No significant body weight change and no difference in testis, seminal vesicle, liver or gonadal fat weights No gross morphological changes in testis No significant change of motile sperm No significant difference in gene expression No effect on seminiferous tubule measurements No effect in the number of proliferating cells or Sertoli Cells	Kolaitis et al. (2023)
120 mg/kg b.w.	Wistar-albino rats	21 days	↓ Weight change, testicular weight and relative testicular weight ↓ Total sperm count ↓ Testosterone level ↓ Testicular protein concentration and levels of glycogen ↓ Spermatogenic activity	Rotimi & Adeyemi (2023)
120 mg/kg	Rats	7 days	↓ gonadal hormonal concentrations, semen quality parameters and testicular function indices ↑ oxidative stress ↓ antioxidant potential ↓ sperm quality ↑ inflammatory markers in brain, testis and epididymis ↑ degeneration histo-architecture in brain, testis and epididymis	Rotimi, Ojo & Adeyemi (2024)
5.4 µg/L	Largemouth Bass (Micropterus salmoides)	6 months	↓ Sperm motility and count ↓ Gonadosomatic index	Leet et al. (2022)

5, 10, 15 and 20mg/l	Crayfish <i>Procambarus</i>	28 days	↑ Mortality ↑ Reproductive hormones of females	Nassar et al. (2022)
	<i>clarkii</i>		↓ Total protein content of the ovary and haemolymph ↓ Testosterone levels in the testis No significant difference in the total protein content of males	
NA	Human sperm	NA	Atrazine's metabolite found in four of the six samples	Rodríguez-Robledo et al. (2022)
2, 10, 70, and 100 mg/kg b.wt/day	Male Rats	21 days	↑ Body weight ↓ Testis weight, epididymis, adrenal and seminal vesicle Delayed sexual maturation ↓ Serum testosterone levels ↑ Serum estradiol levels ↓ Sperm count and motility Testis histology alterations ↓ Fertility potential	Pandey et al. (2021)
ATZ of 0.2 ppm	Caiman <i>latirostris</i>	70 days	Effects on thyroid histoarchitecture	Galoppo et al. (2020)
5 mg/kg bw/day	Mice	12 week cohort 26 week cohort	No effect on the sex ratio of pups, birth weight and survival No difference on body weight, tissue weight and morphology ↓ Epididymal sperm concentration in the 12 week cohort No difference in the epididymal sperm concentration in the 26 week cohort No effect on daily sperm concentration	Harper et al. (2020)
100 mg/kg/day 6.25 and 12.5 mg/kg/day	Mice	21 days	No significant changes in body and testis weight Affected penile morphology and testis descent	Tan et al. (2021)



25 mg/kg BW/day	Rats	12 months	Transgenerational leanpathology in nearly a third of the animals	Thorson et al. (2020)
-----------------	------	-----------	--	-----------------------

## DISCUSSION

### ATRAZINE EFFECTS ON ENDOCRINE SYSTEM

Subfertility and infertility related to decreased sperm quality have increased in recent decades. Hypotheses related to lifestyle, environmental factors, and occupational exposure to endocrine disruptors have been proposed and discussed (Thorson *et al.*, 2020).

Across the analyzed period, an increasing number of studies sought to evaluate the toxicity of atrazine on organic systems, with its impact on fertility being one of the most studied aspects. However, the mechanisms by which atrazine interacts toxically with the human reproductive system appear to be non-uniform, with several pathways potentially involved (Gomes-Andrade *et al.*, 2024; Rotimi & Adeyemi, 2023; Rotimi, Ojo & Adeyemi., 2024; Rodriguez-Robledo *et al.*, 2022). Among these, atrazine as an endocrine and metabolic disruptor is already well characterized (Rotimi & Adeyemi., 2023). However, few studies have evaluated long-term contact, especially prenatal exposure to atrazine, see study carried out by Tan *et al.* (2021) for exceptions. This has been interpreted as cause for concern, as individuals subjected to chronic exposure may have their health impacted more severely (Harper, Finger & Green, 2020).

Analysis of prolonged exposure to atrazine is relevant since recent research indicates that endocrine disruptors from this toxin can bioaccumulate in seminal plasma (Rodríguez-Robledo *et al.*, 2022). This provides new avenues for future investigations into the association between endocrine disruptors bioaccumulated in seminal plasma and infertility. A Spanish study with six semen samples donated by healthy men, identified atrazine metabolites in the seminal plasma of four individuals (Rodríguez-Robledo *et al.*, 2022).

In addition to the detrimental effects on the neuroendocrine system, such as inhibition of the function of the hypothalamic-pituitary-testicular axis, research has also implicated atrazine in the toxification of the gonads, adrenal glands, thyroid axis (including epigenetic changes) (Thorson *et al.*, 2020; Rotimi, Ojo & Adeyemi, 2024; Zhao *et al.*, 2024). Additionally, Rodríguez-Robledo *et al.* (2022) and Galoppo *et al.*, (2020) have described possible associations with atrazine and its bioaccumulation in the body.

In the environment, atrazine can interact with other contaminants and so have its toxic effect augmented, increasing its capacity to negatively impact human health. As an



example of this, a study carried out in the city of Campinas, in the interior of the Brazilian state of São Paulo, analyzed the interaction of atrazine with microplastics in aquatic environments. The presence of microplastics in water was found to be capable of acting as sorption agents, and so capable of increasing the effective concentration of atrazine. The study also reported that atrazine has a greater tendency to remain soluble in water; however, the presence of microplastics reduces this capacity by absorbing it onto the surface of the plastic particles. Thus, the presence of microplastics in water increases the risk of contamination by atrazine, especially because it can be bioaccumulated by humans (Dias *et al.*, 2023).

In another study of atrazine as a water contaminant, Chamot *et al.* (2023) analyzed the effects of this compound on thyroid-stimulating hormone (TSH) newborn children in France. They reported no significant changes in TSH levels compared between groups exposed and not exposed to water contaminated with atrazine. However, in this study, more than half of the samples were below the quantification limit.

Studies involving humans are the exception, as most evaluations of the effects of atrazine on TSH are performed on animals, such as mice and crocodilian. This can make it difficult to extrapolate the results to humans (Gomes-Andrade *et al.*, 2024; Harper, Finger & Green, 2020). However, studies of vertebrate animals exposed to atrazine during embryonic development, have reported that the disruption of the thyroid axis profoundly impacts metabolism and reproduction (Galoppo *et al.*, 2020). Additionally, since thyroid hormone signaling is strongly conserved among vertebrates, it has been suggested that atrazine produces adverse effects in other vertebrates, including humans. Findings of studies of the exposure of broad-snouted caiman eggs to atrazine warn of the impacts that long-term contact can cause (Galoppo *et al.*, 2020).

In the context of environmental exposure and persistence, atrazine's action as an endocrine and metabolic disruptor, this compound causes a decrease in the metabolic activity of reproductive cells, impaired glycolytic function, reduced expression of the enzyme lactate dehydrogenase (LDH), and effects the production and secretion of gonadal androgens (Gomes-Andrade *et al.*, 2024; Rotimi & Adeyemi, 2023; Abarikwu *et al.*, 2023; Hassanin *et al.*, 2024).

## ATRAZINE EFFECTS ON REPRODUCTIVE SYSTEM

By decreasing the expression of LDH, atrazine impairs the glycolytic function of Sertoli cells, directly compromising the nutritional support of spermatogenesis, since this enzyme is responsible for the conversion of pyruvate into lactate, a substrate to nourish germ cells in spermatogenesis (Gomes-Andrade *et al.*, 2024). Indeed, the action of atrazine is sufficiently potent that, at very low concentrations in human biofluids, and at the legal limit in drinking water, atrazine is capable of inhibiting the glycolytic function of Sertoli cells (Gomes-Andrade *et al.*, 2024).

However, the study by Gomes-Andrade *et al.* (2024) used the immortalized murine cellline TM4. This is an important methodological limitation, as such cells do not represent the complexity of Sertoli cells *in vivo*. In addition, the tissue microenvironment and cell-cell interactions that influence the dynamics of Sertoli cells was absent under the deployed experimental.

Another fundamental element in the spermatogenesis process is testosterone, a steroid hormone secreted by Leydig cells, which binds to receptors in Sertoli cells, regulating the function of the epididymis in the storage, maturation, concentration, motility and protection of sperm (Rotimi & Adeyemi, 2023).

A plausible and widely accepted mechanism for how atrazine acts to reduce serum testosterone, is the inhibition of the enzyme  $3\beta$ -hydroxysteroid dehydrogenase ( $3\beta$ -HSD). This enzyme is expressed in the Leydig cells, which are the site of several steps in the steroidogenic cascade that results in the formation of testosterone. As a result, low levels of serum and intratesticular testosterone trigger reproductive disorders that affect spermatogenesis (Abarikwu *et al.*, 2023).

Work on mice by Harper, Finger and Green (2020) found that exposure to atrazine affects the gene expression of steroids in the testes, this occurs because the herbicide produces a significant increase in the expression of the Cyp19a1 gene, which codes for aromatase, the enzyme responsible for converting androgens into estrogens. The study also reported a reduction in sperm concentration, which may be related to hormonal imbalances. In rats and mice, exposure to atrazine can affect sperm cell count, testicular weight, sperm viability and mortality, and also reduce testosterone levels, negatively influencing male fertility (Zhu *et al.*, 2021; Rotimi & Adeyemi, 2023).

Using an endocrine approach Hassanin *et al.* (2024) and Mohammed *et al.* (2023) found that rats subjected to atrazine via gastric tube had reduced fertilization capacity. This

was accompanied by decreased serum testosterone levels, upregulated caspase 3 mRNA levels, increased iNOS mRNA expression, destruction of seminiferous tubules, damage to germinal epithelium, congested and dilated blood vessels, and reduced Leydig cells.

Regarding mitochondria and production of reactive oxygen species (ROS), several studies report a marked increase in oxidative stress and inflammatory markers when exposed to atrazine (Rotimi & Adeyemi, 2023; Abarikwu *et al.*, 2024b; Mohammed *et al.*, 2023). A study carried out by Xiao-Wei Li *et al.* (2024) with granulosa cells from female quail, found that exposure to atrazine decreases cell viability and proliferation, increases oxidative stress and inhibits mitochondrial function-related gene expression. However, a study by Gomes- Andrade *et al.* (2024) observed no changes in either mitochondrial membrane potential or production of reactive oxygen species in Sertoli cells at all atrazine concentrations tested, even though there was a reduction in the metabolic activity of these cells, suggesting that toxic concentrations of atrazine do not specifically affect mitochondrial function or cause oxidative stress in these cells.

As can be seen from the material cited above, collectively, studies have demonstrated that atrazine alters the expression of molecular markers associated with the development and function of germ cells that can be influenced by low testosterone levels. With the suppression of testosterone and defects generated in Sertoli and Leydig cells, atrazine affects fertility directly by inhibiting spermatogenesis and/or decreasing the quality of sperm produced (Anlar *et al.*, 2021; Abarikwu *et al.*, 2023; Rotimi & Adeyemi, 2023; Hassanin *et al.*, 2024; Mohammed *et al.*, 2023, Pandey *et al.* 2021).

Additionally, it can also significantly alter the morphology of the spermatozoon. Studies have reported damaged spermatogonia, irregular contours of the primary spermatocyte nuclei, round spermatids with loss of the acrosomal cap, and a reduced number of spermatozoa in the lumen (Hassanin *et al.*, 2024; Mohammed *et al.*, 2023).

Morphological changes in the reproductive organs, frequently observed with atrazine exposure, are directly related to its toxic effects on fertility. Studies have reported atrazine produces morphological and functional damage to testicular structures, including gonadal atrophy, damage to the seminiferous tubules, and disruption of the germ lines (Rotimi & Adeyemi, 2023, Pandey *et al.* 2021). In addition, abnormal morphology of the urogenital matingbulge (MUMP) in rats, as well as reduction in its size and the occurrence of hypospadias, have been associated with atrazine toxicity (Govers *et al.*, 2019).

Research conducted with male mice (Abarikwu *et al.*, 2024a) indicate that exposure to atrazine can cause acute and irreversible effects on the testes, including damage to Sertoli and germ cells, plus changes in hormone levels, and testicular inflammation. In addition, when the mother mouse is contaminated with atrazine during gestation and lactation, male offspring can develop testicular alterations, resulting in sexual immaturity, histological alterations, subfertility, and cryptorchidism (Govers *et al.*, 2019; Nassar, Mohamed & Said, 2022; Pandey *et al.* 2021, Riera *et al.*, 2022).

Prenatal exposure of rats to 100 mg/kg of atrazine produced changes in anogenital distance, testicular descent, and significantly reduces the size of the glans penis in Offspring. This highlights the cumulative effects, as well as their transgenerationality (Tan *et al.*, 2021).

Whether atrazine exposure can produce a reduction in absolute and relative body weight and reproductive organs has been a topic of discussion between authors. In a study developed by Rotimi and Adeyemi (2023), Wistar rats treated with atrazine (120mg/kg) showed a reduction in the weight of the body, testis and epididymis, as well as a decrease in sperm concentration and semen quality. Mohammed *et al.* (2023), Pandey *et al.* (2021) and Abarikwu *et al.* (2024b) corroborated these findings, emphasizing the role of atrazine in reducing body mass. However, other studies did not find significant differences in the absolute and relative weight of rats exposed to atrazine compared to controls, suggesting the need for further investigations on the impact of the substance on total body mass and reproductive organs (Govers *et al.*, 2019; Harper, Finger & Green, 2020).

Furthermore, a study conducted in Australia on prenatal exposure of rats to 5 mg/kg atrazine did not reveal significant weight gains or differences in the absolute and relative weights of seminal vesicles, testes, and fat pads. However, it did show decreased epididymal sperm concentration in 12-week-old males, suggesting that atrazine exposure may have more pronounced effects in younger males (Harper, Finger & Green, 2020).

While transgenerational effects of atrazine are also of concern, a study using a concentration of 0.02 ng/ml atrazine (considered the conservative average in Australian waters) did not show significant changes in the timing of puberty onset, body weight, testicular morphology, or percentage of motile sperm in two generations of rats (Thorson *et al.*, 2020; Kolaitis *et al.*, 2023).

Other studies, such as those by Carriquiriborde *et al.* (2023) and Leet *et al.* (2022) on fish, suggest that atrazine may affect the health of testicular germ cells, so interfering with

reproductive capacity. In addition, research with the freshwater shrimp *Procambarus clarkii*, found that atrazine caused disturbances in the distribution of spermatogonia and necrosis in the testicular structure, in addition to decreasing testosterone levels (Nassar, Mohamed & Said, 2022).

Sperm motility is one of the main parameters used to assess fertility and reproductive capacity. A reduction in total sperm count, as well as a decrease in motility and the presence of sperm with compromised morphology, including head defects, tail division and membrane ruptures, were observed in rats exposed to atrazine (Rotimi & Adeyemi, 2023; Hassanin *et al.*, 2024). This pattern of impairment was also identified in fish, as demonstrated by Leet *et al.* (2022).

However, it is also important to note that a study of rats by Kolaitis (2023) did not find any significant change in sperm parameters. Sperm are highly sensitive to hormonal changes and, probably, the concentration of atrazine used in this study was insufficient to generate changes in sperm parameters. Therefore, research on the effects of atrazine continues to be a relevant and necessary field to understand its implications on the reproductive health across a variety of different organisms.

In summary, atrazine has significant potential to cause morphological and functional changes in sperm and reproductive structures due to its role as an endocrine disruptor. This makes continuous monitoring and more in-depth studies on its consequences for fertility and reproductive health in different species.

## **FINAL CONSIDERATIONS**

Atrazine is an environmental toxin which many studies have associated with male infertility. Its toxic impact on the reproductive system of animals occurs because the compound causes endocrine dysregulation that leads to changes in hormone concentrations, contributing to alterations in spermatogenesis, metabolic and glycolytic activity of Sertoli and Leydig cells, and histopathological changes in the parenchyma of reproductive organs. In addition, it acts as an inflammatory agent and triggers oxidative stress in the reproductive system.

The toxicity of atrazine on the male reproductive system has been widely discussed and investigated, with studies addressing such aspects as inhibition of the hypothalamic-pituitary-testicular axis, decreased metabolic activity of reproductive cells, impairment of the glycolytic function of Sertoli cells, reduction of enzyme lactate dehydrogenase, decreased

serum and intratesticular testosterone, as well as negative effects on spermatogenesis, and morphological changes in the gonads and sperm as potential pathways for male infertility.

However, some studies have noted difficulties in extrapolating the results obtained from some animal models to humans due to differences in metabolism, lifespan and reproductive system. This also highlights the need for further studies evaluating chronic exposure to atrazine.

Finally, a preventive and dynamic approach to minimize exposure to this toxic compound and a reassessment of regulatory guidelines on the legal limits of atrazine in the environment are essential to preserve the reproductive health of future generations.



## REFERENCES

1. Abarikwu, S. O., Ezim, O. E., Ikeji, C. N., & Farombi, E. O. (2023). Atrazine: cytotoxicity, oxidative stress, apoptosis, testicular effects and chemopreventives interventions. \*Frontiers in Toxicology, 5\*. <https://doi.org/10.3389/ftox.2023.1246708>
2. Abarikwu, S. O., Coimbra, J. L. P., Silva, G. C., Rocha, S. T., Costa, V. V., Lacerda, S. M. S. N., & Costa, G. M. J. (2024a). Acute effects of atrazine on the immuno expressions of sertoli and germ cells molecular markers, cytokines, chemokines, and sex hormones levels in mice tests and epididymides. \*Chemosphere, 363\*. <https://doi.org/10.1016/j.chemosphere.2024.142852>
3. Abarikwu, S. O., Mgbudom-Okah, C. J., Ndufeiya-Kumasi, L. C., Monye, V. E., Aruoren, O., Ezim, O. E., Omeodu, S. I., & Charles, I. A. (2024b). Influence of triazines and lipopolysaccharide coexposure on inflammatory response and histopathological changes in the testis and liver of balb/c mice. \*Heliyon, 10\*. <https://doi.org/10.1016/j.heliyon.2024.e24431>
4. Anlar, H. G., Bacanlı, M., & Basaran, N. (2021). Endocrine disrupting mechanisms and effects of pesticides. \*Arh Farm., 71\*, 480-490. <https://doi.org/10.5937/arhfarm71-34291>
5. Botelho, L. L. R., Cunha, C. A., & Macedo, M. (2011). O método da revisão integrativa nos estudos organizacionais. \*Gestão e Sociedade, 5\*(11), 121-136. <https://doi.org/10.21171/ges.v5i11.1220>
6. Brito, T. P., Aragão, S. S., Souza-Esquerdo, V. F., & Pereira, M. S. (2023). Perfil dos agricultores orgânicos e as formas de avaliação da conformidade orgânica no estado de São Paulo. \*Revista de Economia e Sociologia Rural, 61\*(3). <https://doi.org/10.1590/1806-9479.2022.260825>
7. Carriquiriborde, P., Fernandino, J. I., Lopez, C. G., Benito, E. S., Villagomez, J. M. G., Cristos, D., Trudeau, V. L., & Somoza, G. M. (2023). Atrazine alters early sexual development of the South American silverside, *Odontesthes bonariensis*. \*Aquatic Toxicology, 254\*. <https://doi.org/10.1016/j.aquatox.2022.106366>
8. Centanni, M., Ricci, G. F., Girolamo, A. M., Romano, G., & Gentile, F. (2023). A review of modeling pesticides in freshwaters: current status, progress achieved and desirable improvements. \*Environmental Pollution, 316\*. <https://doi.org/10.1016/j.envpol.2022.120553>
9. Chamot, S., Al-Salameh, A., Petit, P., Bonnetterre, V., Cance, C., Decocq, G., Bouillier, A., Braun, K., & Desailoud, R. (2023). Does prenatal exposure to multiple airborne and top-water pollutants increase neonatal thyroid-stimulating hormone concentrations. \*Science of the Total Environment\*. <https://doi.org/10.1016/j.scitotenv.2023.167089>
10. Chang, J., Fang, W., Chen, L., Zhang, P., Zhang, G., Zhang, H., Liang, J., Wang, Q., & Ma, W. (2022). Toxicological effects, environmental behaviors and remediation



- technologies of herbicide atrazine in soil and sediment: a comprehensive review. *\*Chemosphere*, 307\*(3). <https://doi.org/10.1016/j.chemosphere.2022.136006>
11. Dias, M. A., Batista, P. R., Ducati, L. C., & Montagner, C. (2023). Insights into sorption and molecular transport of atrazine, testosterone, and progesterone onto polyamide microplastics in different aquatic matrices. *\*Chemosphere*, 318\*. <https://doi.org/10.1016/j.chemosphere.2023.137949>
  12. EPA. (2020). Atrazina: caso de decisão de revisão provisória de registro: 0062. Agência de Proteção Ambiental, Washington, DC.
  13. FAO. (2024). *\*The state of food insecurity and nutrition in the world 2024\**. Food and Agriculture Organization of the United Nations, Rome.
  14. Galoppo, H. G., Tavalieri, Y. E., Schierano-Marotti, G., Osti, M. R., Luque, E. H., & Muñoz-De-Toro, M. M. (2020). Long-term effects of in ovo exposure to an environmentally relevant dose of atrazine on the thyroid gland of *\*Caiman latirostris\**. *\*Environmental Research*, 186\*. <https://doi.org/10.1016/j.envres.2020.109410>
  15. Ge, J., Liu, J., Wang, T., Huang, D., Li, J., Zhang, S., & Zhao, L. (2021). Prolonged exposure to the herbicide atrazine suppresses immune cell functions by inducing spleen cell apoptosis in rats. *\*Ecotoxicology and Environmental Safety*, 220\*. <https://doi.org/10.1016/j.ecoenv.2021.112386>
  16. Gomes-Andrade, D., Guerra-Carvalho, B., Carrageta, D. F., Bernardino, R. L., Braga, P. C., Oliveira, P. F., de Lourdes Pereira, M., & Alves, M. G. (2024). Exposure to toxicologically relevant atrazine concentrations impair the glycolytic function of mouse Sertoli cells through the downregulation of lactate dehydrogenase. *\*Toxicology and Applied Pharmacology\**. <https://doi.org/10.1016/j.taap.2024.116929>
  17. Govers, L. C., Harper, A. P., Finger, B. J., Mattiske, D. M., Pask, A. J., & Green, M. P. (2019). Atrazine induces penis abnormalities including hypospadias in mice. *\*Journal of Developmental Origins of Health and Disease*, 11\*(3), 1-4. <https://doi.org/10.1017/S2040174419000473>
  18. Harper, A. P., Finger, B. J., & Green, M. P. (2020). Chronic atrazine exposure beginning prenatally impacts liver function and sperm concentration with multi-generational consequences in mice. *\*Frontiers in Endocrinology*, 11\*. <https://doi.org/10.3389/fendo.2020.580124>
  19. Hassanin, H. M., Kamal, A. A., & Ismail, O. I. (2024). Resveratrol ameliorates atrazine-induced caspase-dependent apoptosis and fibrosis in the testis of adult albino rats. *\*Scientific Reports*, 14\*. <https://doi.org/10.1038/s41598-024-67636-z>
  20. Horzmann, K. A., Lin, L. F., Taslakjian, B., Yuan, C., & Freeman, J. L. (2020). Embryonic atrazine exposure and later in life behavioral and brain transcriptomic, epigenetic, and pathological alterations in adult male zebrafish. *\*Cell Biology and Toxicology*, 37\*, 421-439. <https://doi.org/10.1007/s10565-020-09548-y>

21. Javier, N. (2022). Entisol propiedades químicas en el sistema de agricultura orgánica. *\*International Journal of Science and Society*, 4\*(3). <https://doi.org/10.54783/ij soc.v4i3.513>
22. Lakatos, E. M., & Marconi, M. A. (2003). *\*Fundamentos de metodologia científica\**. São Paulo, SP: Atlas.
23. Leet, J. K., Richter, C. A., Gale, R. W., Tillitt, D. E., & Jenkins, J. A. (2022). Declines in reproductive condition of male largemouth bass (*Micropterus salmoides*) following seasonal exposure to estrogenic endocrine-disrupting compounds. *\*International Journal of Molecular Sciences\**, 23. <https://doi.org/10.3390/ijms232416131>
24. Kolaitis, N. D., Finger, B. J., Merriner, D. J., Nguyen, J., Houston, B. J., O'bryan, M. K., Stringer, J. M., Zerafa, N., Nguyen, N., & Hutt, K. J. (2023). Impact of chronic multi-generational exposure to an environmentally relevant atrazine concentration on testicular development and function in mice. *\*Cells\**, 12, 648. <https://doi.org/10.3390/cells12040648>
25. Martínez-Alfaro, A., & Zuñiga-Orozco, A. (2024). *\*Mucuna pruriens\** (L) DC. peletizada y *\*Tricoderma harzianum\** Rifai aplicados en tomate (*\*Solanum lycopersicum\** L.) como enmienda y biocontrolador. *\*Agronomía Mesoamericana\**, 35. <https://doi.org/10.15517/am.2024.55389>
26. Mohammed, E. T., Safwat, G. M., Bahnasawy, E. A., Abdelyrazik, H. A., & Mohamed, D. S. (2023). Zinc oxide nanoparticles and vitamin C ameliorate atrazine-induced hepatic apoptosis in rat via CYP450s/ROS pathway and immunomodulation. *\*Biological Trace Element Research\**, 201, 5257-5271. <https://doi.org/10.1007/s12011-023-03587-2>
27. Nassar, S. E., Mohamed, A. A., & Said, R. M. (2022). Effects of herbicide atrazine on reproductive hormonal levels, cytochrome P450, and gonadal structure of adult male and female crayfish, *\*Procambarus clarkii\**. *\*Egyptian Journal of Aquatic Biology & Fisheries\**, 26, 1095-1114. <https://doi.org/10.21608/ejabf.2022.279076>
28. Pandey, N., Maske, P., Mote, C., & Dighe, V. (2021). Exposure to atrazine through gestation and lactation period led to impaired sexual maturation and subfertility in F1 male rats with congenital deformities in F2 progeny. *\*Food and Chemical Toxicology\**, 157. <https://doi.org/10.1016/j.fct.2021.112586>
29. Puvvula, J., Bartelt-Hunt, S. L., Ouattara, B. S., Kolok, A. S., Bell, J. E., & Rogan, E. G. (2021). Association between aqueous atrazine and pediatric cancer in Nebraska. *\*Water\**, 13. <https://doi.org/10.3390/w13192727>
30. Riera, J., Matus, E., Matus, L., & Molino, J. (2022). Toxicity of commercial atrazine in *\*Rattus norvegicus\** organs as a function of concentration: Histopathological, ultrastructural and hematological evaluation. *\*An Acad Bras Cienc\**, 94. <https://doi.org/10.1590/0001-3765202220201125>
31. Rodríguez-Robledo, V., Vendrell, A., García-Cifuentes, A., Villaseca-González, N., Guiberteau-Cabanillas, C., Martínez, L. L., Garde, J. J., & Fernández-Santos, M. R.

- (2022). Determination of atrazine and propazine metabolites deemed endocrine disruptors in human seminal plasma by LC–ESI-MS/MS. *\*Chemical and Biological Technologies in Agriculture\**, 9. <https://doi.org/10.1186/s40538-022-00285-4>
32. Rotimi, D. E., Ojo, O. A., & Adeyemi, L. S. (2024). Atrazine exposure caused oxidative stress in male rats and inhibited brain-pituitary-testicular functions. *\*Journal of Biochemical and Molecular Toxicology\**, 38. <https://doi.org/10.1002/jbt.23579>
33. Rotimi, D. E., & Adeyemi, O. S. (2023). Plantain-based diet modulates atrazine-induced testicular toxicities in rats. *\*Asian Pacific Journal of Reproduction\**, 12(4), 170-181. <https://doi.org/10.4103/2305-0500.380984>
34. Sass, J. B., & Colangelo, A. (2006). European Union bans atrazine, while the United States negotiates continued use. *\*International Journal of Occupational and Environmental Health\**, 12(3), 260–267. <https://doi.org/10.1179/oeh.2006.12.3.260>
35. Tan, H., Wu, G., Wang, S., Lawless, J., Sinn, A., Chen, D., & Zheng, Z. (2021). Prenatal exposure to atrazine induces cryptorchidism and hypospadias in F1 male mouse offspring. *\*Birth Defects Research\**, 113, 469-484. <https://doi.org/10.1002/bdr2.1865>
36. Thorson, J. L. M., Beck, D., Maamar, M. B., Nilsson, E. E., McBirney, M., & Skinner, M. K. (2020). Epigenomewide association study for atrazine-induced transgenerational DNA methylation and epigenetic biomarkers of histone retention for illnesses. *\*PLoS One\**, 15(12). <https://doi.org/10.1371/journal.pone.0239380>
37. Vizioli, B. C., Silva, G. S., Medeiros, J. F., & Montagner, C. C. (2023). Atrazine and its degradation products in drinking water source and supply: Risk assessment for environmental and human health in Campinas, Brazil. *\*Chemosphere\**, 336. <https://doi.org/10.1016/j.chemosphere.2023.139289>
38. Vera, Y. M., Carvalho, R. J., Torem, M. L., & Calfa, B. A. (2009). Atrazine degradation by in situ electrochemically generated ozone. *\*Chemical Engineering Journal\**, 155(3), 691-697. <https://doi.org/10.1016/j.cej.2009.09.001>
39. Li, X-W., Guo, K., Wang, C-C., Yang, Y., Li, W., Talukder, M., Li, X-N., & Li, J-L. (2024). The NRF2/ARE pathway as a potential target to ameliorate atrazine-induced endocrine disruption in granulosa cells. *\*Poultry Science\**, 103(6). <https://doi.org/10.1016/j.psj.2024.103730>
40. Zhao, H., Qian, H., Cui, J., Ge, Z., Shi, J., Huo, Y., Zhang, Y., & Ye, L. (2024). Endocrine toxicity of atrazine and its underlying mechanisms. *\*Toxicology\**, 505. <https://doi.org/10.1016/j.tox.2024.153846>
41. Zhu, S., Zhang, T., Wang, Y., Zhou, X., Wang, S., & Wang, Z. (2021). Meta-analysis and experimental validation identified atrazine as a toxicant in the male reproductive system. *\*Environmental Science and Pollution Research\**, 28(28), 37482-37497. <https://doi.org/10.1007/s11356-021-13396-6>