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Reproductive subacute toxicity of the herbicide Clodinafop Propargyl in rabbits male

Toxicidad subaguda reproductiva del herbicida Clodinafop Propargyl en conejos domésticos machos

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ABSTRACT

Several studies have evaluated the reproductive toxicity of herbicides. However, data on the reproductive effects of clodinafop-propargyl remain limited. Therefore, the present study aims to assess the reproductive toxicity of clodinafop-propargyl by evaluating the testicular Subacute toxicity in adult male rabbits using morphometric histological and hormonal parameters. Rabbits aged 5 to 6 months were randomly divided into four groups: three experimental groups (G1, G2, G3) administered increasing doses of Clodinafop Propargyl, and a control group receiving distilled water over four weeks period. Serum hormone levels were determined by enzyme-linked immunosorbent assay analysis, revealing a significant, dose-dependent decline in plasma testosterone levels. Mean testosterone levels were 11.14 ± 0.93 nmol·L^{-1} in the control group, compared to 7.66 ± 0.67 nmol·L^{-1} in G1, 5.75 ± 0.81 nmol·L^{-1} in G2, and 0.95 ± 0.72 nmol·L^{-1} in G3 (P<0.05). Testicular weights also decreased significantly: 9.97 ± 0.88 g in controls, 9.10 ± 4.73 g in G1, 7.83 ± 0.61 g in G2, and 1.03 ± 0.71 g in G3 (P<0.05. Histological assessment of testicular and epididymal tissues was conducted using Hematoxylin and Eosin and Azan's trichrome stains. The result included degeneration of seminiferous tubules, epithelial disorganization, germ cell depletion especially Leydig cells, and increased interstitial collagen deposition, consistent with testicular fibrosis. The highest dose group (G3) showed marked reduction in spermatogenesis and spermatozoa counts in the lumen of seminiferous tubules. These findings indicate that exposure to Clodinafop Propargyl induces dose-dependent structural and functional damage to the testes, with potential implications for male reproductive health and fertility.

Key words: Testicular toxicity; clodinafop-propargyl; morphometry; histopathology; rabbits; reproduction; fibrosis; herbicide exposure

RESUMEN

Varios estudios han evaluado la toxicidad reproductiva de los herbicidas. Sin embargo, los datos sobre los efectos reproductivos del clodinafop-propargil siguen siendo limitados. Por lo tanto, el presente estudio tiene como objetivo evaluar la toxicidad reproductiva del clodinafop-propargil mediante la evaluación de la toxicidad testicular subaguda en conejos machos adultos, utilizando parámetros morfométricos, histológicos y hormonales. Los animales, de 5 a 6 meses de edad, fueron asignados aleatoriamente a cuatro grupos experimentales. El grupo control mostró una ganancia de peso normal durante los 30 días del experimento, mientras que los grupos tratados presentaron retraso en el crecimiento dependiente de la dosis, especialmente en la dosis más alta. Los niveles séricos de hormonas, determinados mediante el ensayo de inmunoadsorción ligado a enzima, mostraron una disminución significativa y dependiente de la dosis en la concentración de testosterona: 11,14 ± 0,93 nmol·L^{-1} en el grupo control; 7,66 ± 0,67 nmol·L^{-1} en G1; 5,75 ± 0,81 nmol·L^{-1} en G2; y 0,95 ± 0,72 nmol·L^{-1} en G3 (P<0,05). El peso testicular también se redujo de manera significativa: 9,97 ± 0,88 g (control), 9,10 ± 4,73 g (G1), 7,83 ± 0,61 g (G2) y 1,03 ± 0,71 g (G3) (P<0,05). El examen histopatológico de testículos y epidídimos reveló lesiones graves y dependientes de la dosis en los grupos G2 y G3, incluyendo atrofia de los túbulos seminíferos, desorganización celular y vacuolización, sin alteraciones en los animales del grupo control. Estos resultados demuestran que el Clodinafop Propargyl induce una toxicidad reproductiva severa en conejos machos, afectando de forma significativa la estructura y función testicular, especialmente a dosis elevadas.

Palabras clave: Toxicidad reproductiva; Clodinafop-propargyl; morfometría; histopatología; conejos; reproducción, fibrosis; exposición a herbicida

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INTRODUCTION

According to the Food and Agriculture Organization (FAO) [1], nearly half of the world's arable land is currently used for agricultural activities. Within this cultivable area, farmers face several biotic stresses, among which weed infestation represents one of the main limitations to crop productivity [1].

Consequently, the use of herbicides has become a crucial component of modern agriculture, significantly contributing to yield improvement and efficient weed management in both cultivated and non-crop areas [2].

Nevertheless, the intensive use of chemicals products like herbicides leads to contamination of soil and water, representing a potential risque to human, animal, and plant health [3].

While herbicides are widely used in modern agriculture and have been extensively studied, important knowledge gaps remain regarding their medium – and long-term effects on non-target organisms. The current study was therefore designed to evaluate the subacute effects of clodinafop-propargyl on male rabbits, with particular attention to its potential reproductive toxicity. clodinafop-propargyl stands out as an active ingredient belonging to the aryloxyphenoxypropionate family (*"fops"*), It is widely applied in cereal crops for post-emergence management of annual grass weeds, including *Avena (Avena sativa)*, *Lolium*, *Setaria*, *Phalaris*, and *Alopecurus* [2].

This herbicide acts by inhibiting the enzyme acetyl-coenzyme A carboxylase (ACCase), which is essential for lipid biosynthesis in plants [1]. Experimental studies have reported sex-related differences in the toxicological response to Clodinafop-propargyl in rats. Male animals exhibited greater systemic exposure compared with females, as indicated by higher plasma concentrations and a slower elimination rate of the compound. This pharmacokinetic profile suggests that males may be more susceptible to the toxic effects of the herbicide.

Reproductive investigations did not indicate any significant impairment of fertility. Nevertheless, developmental effects were observed in the offspring when parental animals were exposed to high doses. These effects included: reduced in pup body weight, delayed physical development, and several morphological alterations, such as incomplete ossification and bilateral ureter torsion [4].

However, the United States Environmental Protection Agency (U.S. EPA) categorizes Clodinafop Propargyl as "likely to be carcinogenic to humans". Toxicity data reported by the U.S. EPA based on studies in rats, mice, rabbits, and dogs indicate that high doses of *clodinafop-propargyl* induce adverse effects such as hepatocellular hypertrophy, liver necrosis, and thymic atrophy [5]. This study aims to evaluate the subacute toxicity of clodinafop-propargyl in rabbits and to determine whether the observed effects corroborate the data reported by the U.S. EPA [5].

Although its extensive use, the available information on the reproductive effects of clodinafop-propargyl and other fop derivatives remains limited. In particular data on aquatic species and mammalian reproduction are sparse. This lack of comprehensive studies highlights the need for further research. The present study was therefore designed to address these gaps and provide updated, reliable evidence to better understand the potential risks associated with these compounds.

By contrast, various studies on other herbicides have demonstrated their ability to cause genotoxicity and disrupt endocrine and reproductive functions in mammals [1, 2], according to the literature, The effectiveness of Clodinafop Propargyl on crops is well documented; however, their effect, specially potential sub chronic toxicity on animal and human health remain a major concern and insufficiently explored [1, 2].

Therefore, the objective of this study is to investigate the subacute reproductive toxicity of the herbicide Clodinafop Propargyl, which contains *clodinafop-propargyl* as its active ingredient, in adult male rabbits (*Oryctolagus cuniculus*). Specifically, this research evaluates its effects on reproduction via serum testosterone levels, and histopathological alterations in testicular and epididymal tissues.

MATERIAL AND METHODS

Animals and experimental design

This study is a continuation of our previous research, Rebahi *et al.* [6]. Healthy adult male domestic rabbits, aged 5–6 months and weighing 2.5–3.0 kg (Kern & Sohn, PCB 5000–2, Germany), were used in this study, administered increasing doses of Clodinafop propargyl (The doses used in this study were selected based on previous toxicological studies and preliminary observations.). The animals were randomly divided into four groups (n = 6 per group) as follows:

- G1: received 1 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC
- G2: received 4 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC
- G3: received 20 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC
- Control group: received distilled water only

The herbicide Topik 80 EC (Syngenta Crop Protection AG, Switzerland), containing 80 % *clodinafop-propargyl* as the active ingredient, was administered orally once daily for 30 consecutive days (which corresponds to the commonly accepted timeframe for subacute toxicity studies) using a calibrated gastric tube. All animals were maintained under standard laboratory conditions (temperature 25 ± 2°C; relative humidity 60 ± 5 %; 12 h light-dark cycle) with *ad libitum* access to food and water.

Hormonal analysis

At the end of the experiment, blood samples were collected from each rabbit into heparinized gel tubes for hormonal assay. Serum was separated by centrifugation using an IKA® Vortex Genius 3 (IKA-Werke GmbH & Co. KG, Germany). 1,000-1,300 × g for 10 min and stored at −80°C in a laboratory freezer (Liebherr, FKv 5120, Germany) until analysis. Serum testosterone concentrations were determined using a commercial enzyme-linked immunosorbent assay (ELISA) kit, following the manufacturer's instructions.

Testicular mass

After the euthanasia of the rabbits at the end of the experimental period (an intravenous administration of an appropriate euthanizing agent to induce rapid central nervous system depression, resulting in cardiac and respiratory arrest. All procedures were carried out by trained personnel to ensure rapid and humane death), the testes were carefully dissected from each rabbit for evaluation and weighed individually using an analytical balance (± 0.001 g) using an analytical balance (OHAUS, POWER,China). The testicular mass was calculated and expressed in $g \cdot kg^{-1}$.

Histopathology

Testicular tissues were fixed in 10 % neutral buffered formalin for histological analysis. After fixation, samples were dehydrated, embedded in paraffin wax, and sectioned at 5 µm thickness using a rotary microtome using Leica Biosystems, RM2125 RTS, Germany.

The tissue sections were stained with hematoxylin and eosin (H&E) and with Masson's trichrome according to the procedure outlined by Cardiff *et al.* [7]. The stained slides were then examined under a light microscope (Leica DM500, Germany) to assess the structure of the seminiferous tubules, the arrangement of germ cells, and the condition of the interstitial tissue.

Statistical analysis

Data were analyzed using one-way analysis of variance (ANOVA) followed by Türkiye post hoc test (to compare between groups) ($P<0.05$ considered significant).

RESULTS AND DISCUSSION

Impact of Clodinafop Propargyl on the endocrine system (testosterone levels)

Serum testosterone levels showed a clear dose-dependent decline (TABLE I), with all herbicide-treated groups differing significantly from the control. (a marked decline in G3 ($P<0.05$)).

Endocrine disruption in testicular cells can have detrimental effects on the reproductive system, including epigenetic changes that may be transmitted to offspring [8]. Specifically, such disruption may lead to a decrease in sperm count and production in adulthood, reduced serum testosterone levels during puberty, and an increased number of abnormal spermatozoa in rats [9].

Analysis of variance results showed a marked difference between the groups ($P<0.000$) (TABLE II), which was further confirmed by post hoc tests.

TABLE I
Mean Plasma Testosterone Levels ($nmol \cdot L^{-1}$) in Control and Treated Rabbit Groups (Mean ± SD)

Group	Control	G1	G2	G3
Testosterone ($nmol \cdot L^{-1}$)	11.14 ± 0.93	7.66 ± 0.67	5.75 ± 0.81	0.95 ± 0.72

G1: received 1 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC, G2: received 4 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC, G3: received 20 $mg \cdot kg^{-1} \cdot day^{-1}$ of Topik 80 EC, Control group: received distilled water only

TABLE II
Analysis of variance of plasma testosterone variation among groups

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F	*P*–value (Sig.)
Between groups	298.74	3	99.58	159.70	0.000***
Within groups	11.22	18	0.62	–	–
Total	309.96	21	–	–	–

The administration of Clodinafop Propargyl to adult male rabbits caused a significant reduction in serum testosterone levels in the group 2 treated with 4 $mg \cdot kg^{-1}$, however a more pronounced decrease observed in the group receiving high dose 20 $mg \cdot kg^{-1}$ after one month of treatment. This reduction may affect spermatogenesis process, potentially explaining the morphological and functional alterations observed in reproductive organs (the testes and epididymis).

Several studies showed the inhibitory effects of pesticides on secretion of hypothalamic-pituitary-gonadal axis. it was also confirmed that they have an anti-androgenic effect, which leads to a decrease in these hormonal secretions [10], this confirms the present results.

These findings are further supported by both macroscopic and histological observation of the testes and epididymis, as well as semen quality analysis (spermogram), which revealed abnormalities in parameters including sperm motility, speed, concentration, and viability in Clodinafop Propargyl – treated rabbits.

Other study by Yousef *et al.* [11], demonstrated that exposure to glyphosate (G) adversely affected male rabbit reproductive health, reporting reductions in body weight.

Additionally, research by Clair *et al.* [12] investigated the effects of glyphosate and its formulation on fresh testicular cells from mature rats. They reported that even at low, non-toxic concentrations (1 ppm), exposure to glyphosate and its commercial formulation Roundup led to a decrease in testosterone levels, highlighting that endocrine disruption can occur at environmentally relevant doses of herbicide.

Effects of Clodinafop Propargyl on testicular weight and histopathological structure in male rabbits

The testes are particularly sensitive to xenobiotics, and exposure to such compounds whether through food, water, or air can disrupt endocrine function and adversely affect the male reproductive system, especially the testicular tissue [8, 13]. A significant reduction ($P<0.05$) in testicular weight and dimensions was observed in G2 and G3 groups compared to control, no changes were observed in G1 treated with the low dose (TABLES III and IV).

A marked overall difference was detected among the four groups ($P<0.01$). Group 1 showed a non-significant reduction in testicular weight relative to the control ($P>0.05$). In contrast, G2 and G3 exhibited a highly significant decrease compared with the control group ($P<0.01$). Significant differences were also observed between G1 and group G3, as well as between G2 and G3 ($P<0.01$). Moreover, testicular weight in G1 was significantly lower than in G2 ($P<0.05$).

TABLE III
Variation in testicular weight in control and treated rabbits exposed to three doses of Topik 80 EC (ANOVA)

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F	*P*–value (Sig.)
Groups	61.8333	3	60.6111	44.0095	5.39×10^{-9}***
Error	9.3667	20	0.4683	–	–

TABLE IV
Tukey HSD Post-Hoc test for pairwise comparisons of testicular weight between rabbit groups

Groups Compared	Tukey HSD Q Statistic	*P*–value	Inference
Control vs. Group G1	3.1021	0.1593	Not significant
Control vs. Group G2	7.6358	0.0010	*P*<0.01 (significant)
Control vs. Group G3	15.2717	0.0010	*P*<0.01 (significant)
G1 vs. G2	4.5338	0.0212	*P*<0.05 (significant)
G1 vs. G3	12.1696	0.0010	*P*<0.01 (significant)
G2 vs. G3	7.6358	0.0010	*P*<0.01 (significant)

In the present study, subacute administration of Clodinafop Propargyl resulted in a marked reduction in testicular weight, with signs of atrophy observed at higher doses. This observation aligns with findings as stated by European Food Safety Authority in its 2020 report [14], which reported that Clodinafop-Propargyl exposure in male mice led to reductions in body and testicular weight, as well as testicular atrophy.

In the same way, studies by Abarikwu *et al.* [15] and Khozimy *et al*. [16] demonstrated that Atrazine herbicide exposure after only seven d of treatment showed significantly declined the weight of reproductive organs in rats. However, contrasting evidence was provided by Oliveira *et al.* [17], who reported no significant changes in testicular weight following Roundup™ exposure in male ducks. The observed weight loss in the present study may be directly related to impaired spermatogenesis, but other factors-such as hepatic dysfunction [18, 19] or hormonal imbalances could also contribute. In accordance with these findings, these data revealed a significant reduction in serum testosterone levels following Clodinafop Propargyl exposure, corroborated by histopathological changes in the seminiferous tubules.

Histological findings

Under a light microscope (FIG. 1) reveals the rabbits in groups G2 and G3 (A, B and C) presented histopathological alterations, including structural disorganization, seminiferous tubule atrophy, cellular necrosis, hypocellularity, and cytoplasmic vacuolization.

The rabbits observed in the control group or in group G1 E, F (H&E, 100x) and G (H&E, 40x) where rabbits exhibited the typical anatomical organization of the testes, They were characterized by seminiferous tubules containing fully mature spermatozoa stored. The tubules exhibited a well-organized germinal epithelium, narrow intertubular spaces, and intact interstitial tissue with normal cell populations.

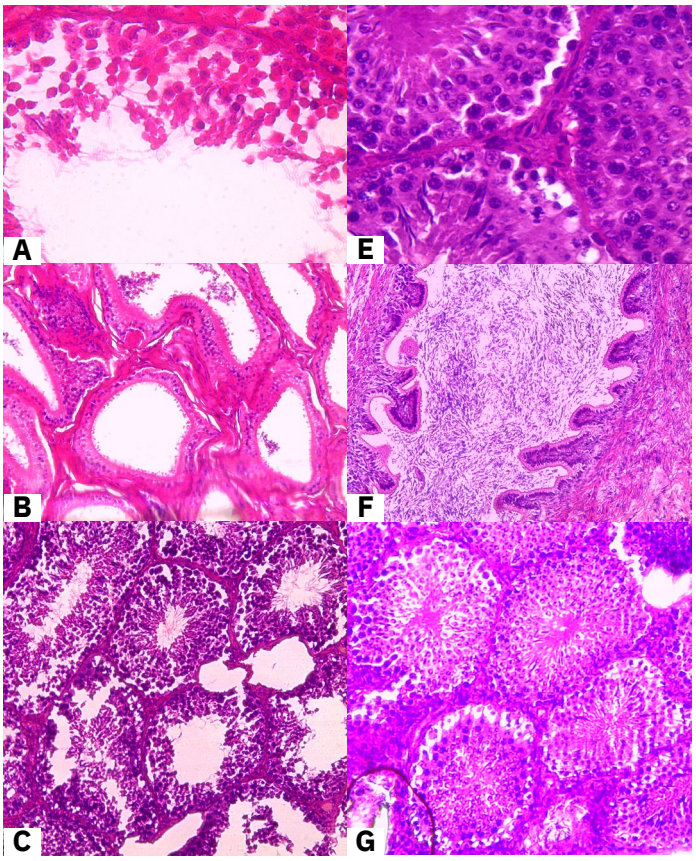

FIGURE 1. A photomicrograph of testicular tissue in treated rabbits B, C (H&E, 40x) and A (H&E, 100x). Revealed pronounced morphological and structural abnormalities within the testes, including a notable reduction in the number of Leydig cells and the diameter of the seminiferous tubules. This narrowing of the tubular lumen was particularly evident at higher exposure levels, E, F (H&E, 100x) and G (H&E, 40x) in control group

Damage to the testicular structure may result either from a direct cytotoxic effect, which explains the progressive reduction in cell number, or from endocrine disruption leading to decreased testosterone levels. Consequently, the absence of the spermatogenesis process results in cellular degeneration and organ atrophy. Comparable alterations were observed by Ahmed *et al.* [10] in male rats administered clodinafop-propargyl baits, including degradation of spermatogenic components, luminal coagulation, and Leydig cell hyperplasia.

Overall, these results are further supported by the work of Mathias *et al*. [20], who reported epithelial alterations in seminiferous tubules following exposure to metolachlor in Wistar rats (*Rattus norvegicus*). Likewise, Moseley *et al.* [21] described negative impacts on fertility indices and structural damage to the reproductive organs (ovarian and uterine tissues) in female rats, exposed to the herbicides glyphosate and atrazine.

In contrasted of the present study suggest that exposure to Clodinafop-propargyl may influence reproductive parameters. Williams *et al.* [22] reported no adverse reproductive effects in animals exposed to glyphosate in chronic and subchronic studies. However, Romano *et al*. [23] observed endocrine and reproductive toxicity associated with glyphosate-based herbicide Roundup Transorb™.

In this study, a dose-dependent narrowing and deformation of the tubular lumen were consistently observed across all treated groups, with the highest severity seen at the highest dose. Such changes could result from a decline in seminiferous tubule activity. The germinal epithelium exhibited degenerative features, including a reduced population of germ cells and frequent necrosis within the seminiferous tubules.

In certain cases, complete loss of luminal content and severe tubular atrophy were evident. Similar degenerative changes were reported by the research of Olayinka and Ore [24] following exposure to the herbicide Haloxyfop-P-Methyl Ester, including severe interstitial edema, necrosis of germinal epithelial cells, and the presence of immature germ cells and cell aggregates within the tubular lumen.

Comparable histological damage has been described in studies of other AOPP herbicides, including fluazifop-p-butyl and phenoxyacetic acid derivatives [25, 26]. In line with these findings, these results show that the degeneration of spermatogenic elements significantly reduced germ cell density. Cytoplasmic vacuolization and detachment of germinal cells from the basal lamina were frequently observed.

Additionally, Sertoli cells exhibited vacuolization and a decline in their supporting role for spermatogenesis, accompanied by disorganization of spermatogonia and developing spermatocytes. Interstitial cell damage, including Leydig cell degeneration and interstitial edema, was prominent. Loss of spermatocytes and increased apoptotic activity contributed to the depletion of elongating spermatids.

Further supporting these observations, Kumawat [27] reported that subacute oral mancozeb exposure led to severe histopathological abnormalities, Similarly, Ksheerasaga and Kaliwal [28], in a study on the temporal effects of mancozeb on testes, accessory reproductive organs, and biochemical constituents in albino mice, showed that testicular and prostate gland weights were significantly decreased after 20 and 30 days of treatment, these effects coincide with hematological alterations previously reported by Rebahi *et al.* [6], highlighting the systemic toxicity of these agrochemicals.

CONCLUSION

After four weeks, the administration of Clodinafop Propargyl on rabbits induced a dose-dependent toxic effects on the male reproductive system. Testes showed a marked decline in weight, and a morphological alteration was observed consisting of histopathological changes with a reduction in Leydig and Sertli cells number, Additionally, a significant reduction in serum testosterone levels, reproductive toxicity was pronounced at higher doses, with testicular atrophy observed in group treated by high dose, present a severe histological damage.

Future studies should aim to elucidate the underlying molecular mechanisms driving this toxicity, assess the reversibility of these effects, and explore potential long-term consequences on reproductive health and transgenerational outcomes.

Conflict of interest

The authors declare that this research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

BIBLIOGRAPHIC REFERENCES

[1] Curran WS. Persistence of herbicides in soil. Crops Soils. [Internet]. 2016; 49(5):16–21. doi: https://doi.org/gn8n9z

[2] Cobb AH. Herbicides and plant physiology. 3rd ed. New York (USA): Wiley-Blackwell; 2022.

[3] Bordjiba O, Ketif A. Effet de trois pesticides (hexaconazole, bromuconazole et fluazifop-p-butyl) sur quelques métabolites physio-biochimiques du blé dur: *Triticum durum.* Desf [Effect of three pesticides (hexaconazole, bromuconazole and fluazifop-p butyl) on some biochemical metabolites of the hard wheat: *Triticum durum*. Desf]. Eur. J. Sci. Res. [Internet]. 2009 [cited 22 Dec 2025]; 36(2):260–268. French. Available in: https://goo.su/m26wN3

[4] European Food Safety Authority (EFSA), Arena M, Auteri D, Barmaz S, Brancato A, Brocca D, Bura L, Carrasco-Cabrera L, Chiusolo A, Civitella C, Court-Marques D, Crivellente F, Ctverackova L, De Lentdecker C, Egsmose M, Erdos Z, Fait G, Ferreira L, Greco L, Ippolito A, Istace F, Jarrah S, Kardassi D, Leuschner R, Lostia A, Lythgo C, Oriol-Magrans J, Medina P, Mineo D, Miron I, Molnar T, Padovani L, Parra-Morte JM, Pedersen R, Reich H, Sacchi A, Santos M, Serafimova R, Sharp R, Stanek A, Streissl F, Sturma J, Szentes C, Tarazona J, Terron A, Theobald A, Vagenende B, Van Dijk J, Villamar-Bouza L. Peer review of the pesticide risk assessment of the active substance clodinafop (variant evaluated clodinafop-propargyl). EFSA J. 2018; 16(11):e05467. doi: https://doi.org/qz8x

[5] Gui W, Dong Q, Zhou S, Wang X, Liu S, Zhu G. Waterborne exposure to clodinafop-propargyl disrupts the posterior and ventral development of zebrafish embryos. Environ. Toxicol. Chem. 2011; 30(7):1576–1581. doi: https://doi.org/cnwjw5

[6] Rebahi S, Alouani A, Meguini-Mohamed N, Khenenou T, Fares MA, Chikha M. Morphometric changes in internal organs and hematological alterations induced by clodinafop-propargyl exposure in domestic rabbits. Int. J. Environ. Sci. [Internet]. 2025 [cited 22 Dic 2025]; 11(3):417–425. Available in: https://goo.su/LuzyvQw

[7] Cardiff RD, Miller CH, Munn RJ. Manual hematoxylin and eosin staining of mouse tissue sections. Cold Spring Harb. Protoc. [Internet]. 2014; 2014(6):655–658. doi: https://doi.org/gjjr83

[8] Anway MD, Memon MA, Uzumcu M, Skinner MK. Transgenerational effect of the endocrine disruptor vinclozolin on male spermatogenesis. J. Androl. [Internet]. 2006; 27(6):868–879. doi: https://doi.org/b4c5jf

[9] Dallegrave E, Mantese FD, Oliveira RT, Andrade AJ, Dalsenter PR, Langeloh A. Pre – and postnatal toxicity of the commercial glyphosate formulation in Wistar rats. Arch. Toxicol. [Internet]. 2007; 81:665–673. doi: https://doi.org/b6dv5z

[10] Ahmed HY, Kandil RA, El-Abd NM. Hepatorenal and testicular dysfunctions of clodinafop-propargyl bait in male black rat (*Rattus rattus*) and its field efficiency. Egypt. Acad. J. Biol. Sci. B Zool. [Internet]. 2023; 15(1):105–118. doi: https://doi.org/qz85

[11] Yousef MI, Salem MH, Ibrahim HZ, Helmi S, Seehy MA, Bertheussen K. Toxic effects of carbofuran and glyphosate on semen characteristics in rabbits. J. Environ. Sci. Health B. [Internet]. 1995; 30(4):513534. doi: https://doi.org/bq6jdm

[12] Clair É, Mesnage R, Travert C, Séralini GE. A glyphosatebased herbicide induces necrosis and apoptosis in mature rat testicular cells in vitro, and testosterone decrease at lower levels. Toxicol. Vitro [Internet]. 2012; 26(2):269279. doi: https://doi.org/d826r9

[13] Savitz DA, Arbuckle T, Kaczor D, Curtis KM. Male pesticide exposure and pregnancy outcome. Am. J. Epidemiol. [Internet]. 1997; 146(12):10251036. doi: https://doi.org/gjvrtw

[14] European Food Safety Authority (EFSA), Silano V, Barat-Baviera JM, Bolognesi C, Chesson A, Cocconcelli PS, Crebelli R, Gott DM, Grob K, Lampi E, Mortensen A, Steffensen IL, Tlustos C, Van Loveren H, Vernis L, Zorn H, Castle L, Di Consiglio E, Franz R, Hellwig N, Kolf-Clauw M, Milana MR, Pfaff K, Volk K, Rivière G. Safety assessment of the substance N,N-bis (2–hydroxyethyl) stearylamine partially esterified with saturated C16/C18 fatty acids, for use in food contact materials. EFSA J. [Internet]. 2020; 18(3):e06047. doi: https://doi.org/qz9b

[15] Abarikwu SO, Adesiyan AC, Oyeloja TO, Oyeyemi MO, Farombi EO. Changes in sperm characteristics and induction of oxidative stress in the testis and epididymis of experimental rats by a herbicide, atrazine. Arch. Environ. Contam. Toxicol. [Internet]. 2010; 58(3):874882. doi: https://doi.org/chwr75

[16] Khozimy AM, ElDanasoury H, Abuzeid M. Biochemical effects of treatments with herbicide atrazine in male albino rats. J. Adv. Agric. Res. [Internet]. 2022; 27(1):4357. doi: https://doi.org/qz9c

[17] Oliveira AG, Telles LF, Hess RA, Mahecha GAB, Oliveira CA. Effects of the herbicide Roundup on the epididymal region of drakes *Anas platyrhynchos*. Reprod. Toxicol. [Internet]. 2007; 23(2):182191. doi: https://doi.org/dgx5dm

[18] CastillaCortázar I, Diez N, GarcíaFernández M, Puche JE, DiezCaballero F, Quiroga J, DíazSánchez M, Castilla A, DíazCasares A, VarelaNieto I, Prieto J, GonzálezBarón S. Hematotesticular barrier is altered from early stages of liver cirrhosis: effect of insulinlike growth factor 1. World J. Gastroenterol. [Internet]. 2004; 10(17):25292534. doi: https://doi.org/qz9d

[19] López-Lemus UA, Garza-Guajardo R, Barboza-Quintana O, Rodríguez-Hernandez A, García-Rivera A, Madrigal-Pérez VM, Guzmán-Esquivel J, García-Labastida LE, Soriano-Hernández AD, Martínez-Fierro ML, Rodríguez-Sánchez IP, Sánchez-Duarte E, Cabrera-Licona A, Ceja-Espiritu G, Delgado-Enciso I. Association between nonalcoholic fatty liver disease and severe male reproductive organ impairment (germinal epithelial loss): study on a mouse model and on human patients. Am. J. Mens Health. [Internet]. 2018; 12(3):639648. doi: https://doi.org/qz9f

[20] Mathias FT, Romano RM, Sleiman HK, de Oliveira CA, Romano MA. Herbicide metolachlor causes changes in reproductive endocrinology of male Wistar rats. Int. Sch. Res. Notices. [Internet]. 2012; 2012:130846. doi: https://doi.org/gb7qhk

[21] Moselhy WA, Nabil TM, AbdelHalim BR, Helmy NA. Effect of atrazine and glyphosate on the reproductive system of female rats: histological and immunohistochemical studies. Assiut Vet. Med. J. [Internet]. 2016; 62(148):101111. doi: https://doi.org/gj5xdq

[22] Williams GM, Kroes R, Munro IC. Safety evaluation and risk assessment of the herbicide Roundup and its active ingredient, glyphosate, for humans. Regul. Toxicol. Pharmacol. [Internet]. 2000; 31(2):117165. doi: https://doi.org/bsb9dn

[23] Romano RM, Romano MA, Bernardi MM, Furtado PV, Oliveira CA. Prepubertal exposure to commercial formulation of the herbicide glyphosate alters testosterone levels and testicular morphology. Arch. Toxicol. [Internet]. 2010; 84(4):309317. doi: https://doi.org/cwbk4x

[24] Olayinka ET, Ore A. Hepatotoxicity, nephrotoxicity and oxidative stress in rat testis following exposure to haloxyfoppmethyl ester, an aryloxyphenoxypropionate herbicide. Toxics [Internet]. 2015; 3(4):373389. doi: https://doi.org/gv8zg7

[25] Ore A, Olayinka ET. Fluazifop-*p*-butyl, an aryloxyphenoxypropionate herbicide, diminishes renal and hepatic functions and triggers testicular oxidative stress in orally exposed rats. Toxicol. Ind. Health [Internet]. 2017; 33(5):406415. doi: https://doi.org/g35z7z

[26] Joshi SC, Tibrewal P, Sharma A, Sharma P. Evaluation of toxic effect of 2,4D (2,4 dichlorophenoxyacetic acid) on fertility and biochemical parameters of male reproductive system of albino rats. Int. J. Pharm. Pharm. Sci. [Internet]. 2012 [cited 22 Sept 2025]; 4(3):338342. Available in: https://goo.su/2aIIyaI

[27] Kumawat S. Evaluation of mancozeb induced subacute oral toxicity in rats [master's thesis on the Internet]. Ludhiana (India): Guru Angad Dev Veterinary and Animal Sciences University; 2020 [cited 22 Sept 2025]. Available in: https://goo.su/5KPBA

[28] Ksheerasagar RL, Kaliwal BB. Temporal effects of mancozeb on testes, accessory reproductive organs and biochemical constituents in albino mice. Environ. Toxicol. Pharmacol. [Internet]. 2003; 15(1):9–17. doi: https://doi.org/fcz4hx