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EFFECTS OF DIFFERENT DOSES OF POTASSIUM DICHROMATE ON MALE FERTILITY AND LIVER TISSUE IN PREPUBERTAL RATS

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ABSTRACT

Chromium is a naturally occurring heavy metal, and its hexavalent form (Cr (VI)) is particularly toxic. Potassium dichromate ($K_2Cr_2O_7$) is one of the most commonly used Cr (VI) compounds in various industries, posing serious environmental risks. The toxicological consequences of acute exposure to varying doses of potassium dichromate were examined in male rats. Following six weeks, fertility-related experiments were conducted to evaluate both testicular and liver changes, biochemical alterations, and reproductive parameters. Histological sections were further analyzed to assess the influence of potassium dichromate on lipid profiles, liver enzyme activities, and reproductive functions. The present findings revealed marked adverse effects on male reproductive health, including reduced fertility and structural alterations in testicular and liver tissues across the tested dose levels. These outcomes suggest that hexavalent chromium compounds may play a contributing role in the global rise of male infertility. Thus, when addressing challenges related to male reproductive health, environmental factors such as exposure to potassium dichromate must be taken seriously into consideration.

KEYWORDS: Potassium Dichromate, Rat, Testes, Fertility, Lipid.

INTRODUCTION

Chromium (Cr) naturally exists in rocks, volcanic emissions, soils, plants, and animals, but it is regarded as a harmful element.[1] It is widely used in stainless steel production, paints, and

metal plating. Among its forms, hexavalent chromium (CrVI) is the most commonly applied, yet it poses significant health risks when released into the environment without proper control.[2] Once inside the cell, CrVI is converted into the trivalent state (CrIII). This conversion lowers its harmful effects, since the trivalent form does not readily interact with vital intracellular macromolecules. Chromium compounds are highly persistent in the environment, resisting natural biodegradation and accumulating to levels that lead to toxic and mutagenic effects.[3] Hexavalent chromium (CrVI) is particularly recognized for its potential to cause carcinogenic outcomes and other harmful impacts on both animals and humans, including allergic dermatitis.[4] The environmental behavior and toxicity of chromium largely depend on its oxidation state.[5] CrVI, is one of the eight metals listed by the U.S. Food and Drug Administration and the Agency for Toxic Substances and Disease Registry among the 50 most hazardous substances[6], poses significant risks when released. Increasing industrial use and improper disposal practices have led to rising levels of chromium in soil, air, and water.[7] In Southeast Asia, the leather tanning industry is a major source of Cr contamination, putting workers at considerable health risk.[8] Moreover, environmental and public health experts warn that chromium pollution in Calaveras Lake threatens the safety of fish consumption for sailors, anglers, and local communities.[9] Like other hexavalent chromium (CrVI) compounds, potassium dichromate is classified as carcinogenic and therefore requires strict adherence to health and safety precautions during handling. Human exposure to CrVI has been associated with adverse outcomes such as reduced fetal viability, genetic mutations, and developmental harm to unborn children. A previous study evaluated the toxic effects of potassium dichromate across various mouse tissues.[10] This compound, one of the most common soluble forms of CrVI, is believed to induce follicular atresia in rodents.[11] Once in the body, chromium is absorbed primarily through the gastrointestinal tract and alveoli, with minimal uptake occurring via the skin.[12] For the general population, oral ingestion— mainly through contaminated food and beverages—is considered the principal route of chromium exposure. Notably, trivalent chromium (CrIII) demonstrates far lower absorption efficiency than CrVI, regardless of the exposure pathway.[13,14] Once hexavalent chromium (CrVI) enters the cell, it undergoes a reduction cascade mediated by cellular reductants such as serum proteins, riboflavin, ascorbic acid, and Cr itself.[15] This sequential reduction generates unstable intermediates, including Cr(V) and Cr(IV). During this process, the reduced products bind to intracellular proteins, causing a transient increase in the chromium content of blood cells.[16]

Concurrently, Cr intermediates promote the production of reactive oxygen species (ROS), leading to oxidative stress. Previous research has demonstrated that Cr(VI), as a potent oxidizing agent, induces extensive cellular injury and structural damage.[17] Elimination of chromium from the body primarily occurs via the biliary and fecal routes, with additional excretion through the kidneys.[18] Hexavalent chromium (CrVI) compounds are designated as Group I human carcinogens[19], a classification supported by strong evidence of their mutagenic and genotoxic effects, as well as the elevated incidence of lung cancer in both humans and animals following inhalation, the primary route of exposure. Although research on the effects of chromium on male reproductive function is limited, available animal studies reveal that murine and rat models exposed to CrO_3 (CrVI) consistently show increased spermatozoa abnormalities.[20] Another frequently observed outcome is a decline in sperm concentration, reported in rats rodents[21,22], Bonnet monkeys[23], and rabbits[24] administered potassium dichromate. Additionally, studies have shown that the unstable chromium intermediate [Cr(V)] exerts damaging effects on the testicular epithelium of rodents.[25] Given the scarcity of comprehensive data, further investigations combining physiological and histological assessments are necessary to clarify the impact of potassium dichromate on sperm function and male fertility in rats. Animal studies investigating the effects of chromium on sperm function have reported a higher incidence of spermatozoa abnormalities in rats and mice exposed to CrO_3 (CrVI).[26] Sperm concentration is another parameter commonly affected, showing a tendency to decrease following chromium exposure. Furthermore, previous research has demonstrated that the chromium intermediate [Cr(V)] impairs the functionality of testicular epithelium and sperm cells in mice.[25] Due to the limited knowledge regarding the impact of potassium dichromate on reproductive cell function and male rat fertility, further investigation is warranted. Therefore, the present study was undertaken to evaluate the reproductive performance and fertility of male rats subjected to different doses and exposure durations of potassium dichromate ($K_2Cr_2O_7$).

METHODOLOGY

Experimental Design

Animals: The laboratory rat, Rattus norvegicus, belongs to the order Rodentia and family Muridae aged 3 weeks were used in the present study. Animals were bred in the animal house of Science College, Cihan University under controlled temperature, 22±2 C°, at (12) hours light and[12] hours dark. The rats were housed in plastic cages measuring 30×12×11 cm.

The total number of animals used in this study was (21) males and (42) females. Males are divided into three categories.

1. Intact male rats received tap water as the control for the experimental categories (N = 7).
2. Intact male rats received 1000 mg/kg of K2Cr2O7. (N=7)
3. Intact male rats received 2000 mg/kg of K2Cr2O7. (N=7)

Fertility experiments: At the end of administration, fertility was determined in male rats exposed for 6 weeks to different concentrations of Potassium Dichromate and tap water. Each male rat is placed in a cage with two intact virgin females of the same strain. The animals were left together for two estrous cycles. Ten days after the removal of the treated male rats, females were killed then the number of pregnant females and the number of fetuses were recorded for each experiment and the following parameters were measured.

Changes in histological structures of testes and liver tissues, biochemical evaluation includes Lipid profiles and Liver enzymes, number of pregnant females and their viable fetuses.

Specimens Collection: At the end of the experiment, animals are anesthetized with chloroform to open the abdomen and remove the liver and testis for histological studies.

Blood Collection: Before killing the animals, blood was withdrawn directly via heart puncture. The blood is placed in an EDTA tube (containing a coagulation inhibitor) for measuring different physiological parameters.

Preparation of Histological sections

Ordinary histological sections were prepared from testes and liver to study any histological changes that may have occurred in the experimental groups after administration of Potassium Dichromate. The rats were sacrificed, and organs were processed according to Homady *et. al*. (2022).[27]

Statistical Analysis

Results were expressed as the mean ± standard deviation (S.D). Data for multiple variable comparisons were analyzed by one-way analysis of variance (ANOVA). For the comparison of significance between groups, Duncan's test was used as a post hoc test according to the statistical package program (SPSS version 16.0) the p values $P< 0.05$ was considered as significant for all statistical analysis in this method.

RESULTS

Biochemical tests

The results of Table 1 and Figure 1 for TG, TC, HDL, LDL, VLDL, GOT, GPT, and ALP levels didn't show any significant changes as compared with the control subjects.

Table 1: Showing the values of liver function markers in male rats from various experimental groups.

Parameters	Mean ± SD							
	TG mg/dl	TC mg/dl	HDL mg/dl	_LDL (u mg/dl	VLDL mg/dl	GOT mg/dl	GPT mg/dl	ALP mg/dl
Control	**42.3∓6.8**	**55∓2**	**39.66∓4.72**	**25.46∓1.3**	**11.2∓0.7**	**162∓ 6,4**	**55.33∓7,57**	**256,33∓11.8**
Treated with 1000 mg/kg of k2Cr2O7	64.33∓8.6	51.66∓1.5	33.33∓1.5	16.53∓1.71	12.86∓1.72	134∓2	52∓3	277,33∓ 131.6
Treated with 2000 mg/kg of k2Cr2O7	45.66∓18.8	69.66∓5.50	43.66∓ 4.40	12.7∓4.97	9.46∓3.93	201∓46	85.33∓18.17	334.33∓57.1

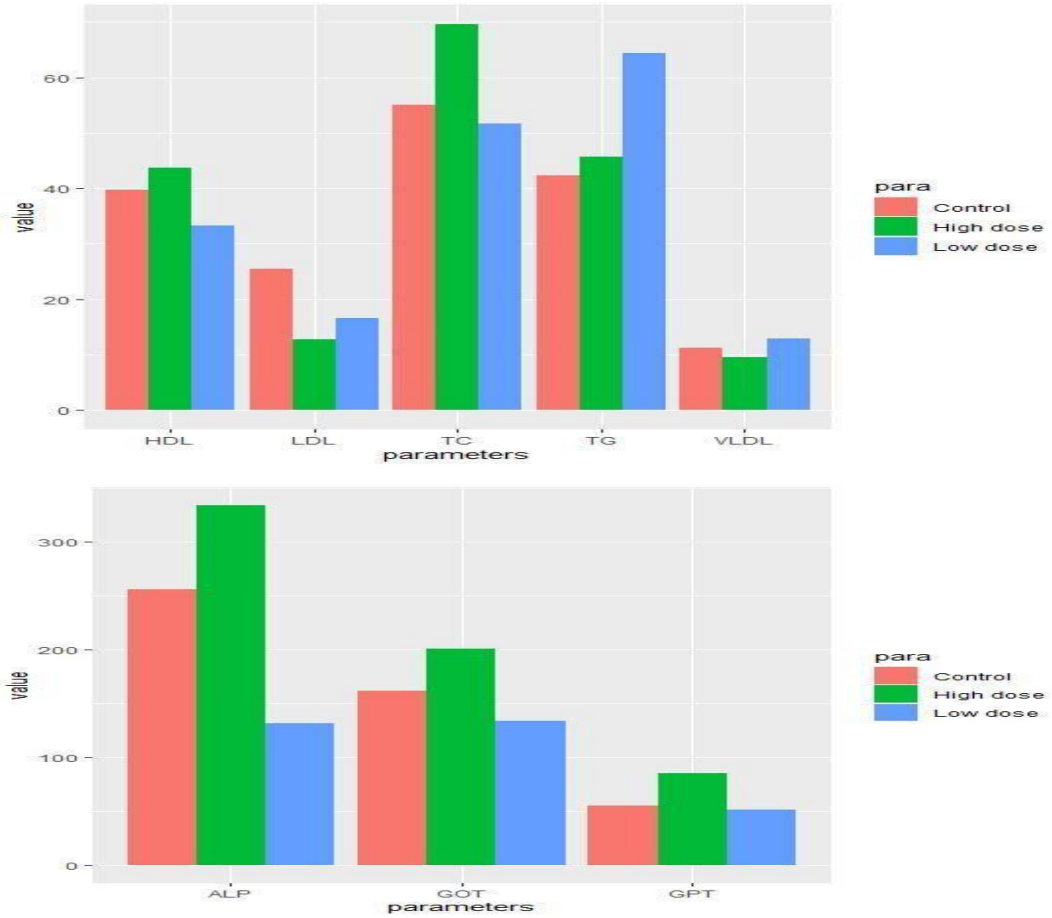

Figure 1: Showing the levels of different liver parameters in different experimental groups after six weeks of treatment.

Fertility: Significant differences (P< 0.05) were observed in the fertility parameters of the treated groups, specifically in the number of pregnant females and the number of implantation sites (Table 2).

Table 2: Showing the impact of various doses of potassium dichromate on male rats after six weeks of treatment.

Doses Mg/kg	Number of males	Number of females	Number of pregnant (%)	Number of implantation sites
control	7	14	92.86% {13]	125
1000 mg/kg of k2Cr2O7	7	14	42.86% {6}	36
2000 mg/kg of k2Cr2O7	7	14	21.43% {3}	17

Histological Results

The histological sections of testes from the contact control group (Figures 1 and 2) revealed densely arranged seminiferous tubules (blue arrow), separated by interstitial tissue containing Leydig cells and blood vessels (black arrow). The spermatogenic series consisted of spermatogonia (SG), primary spermatocytes (SC), spermatids (SD), and spermatozoa (SZ).

Sertoli cells (S) were observed along the basement membrane, characterized by their large, pale nuclei **(**H&E stain).

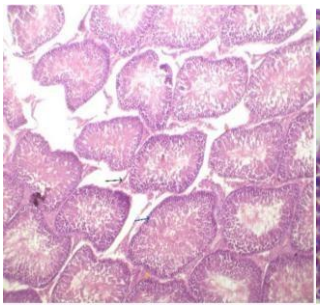

Figure (2) (x 200)

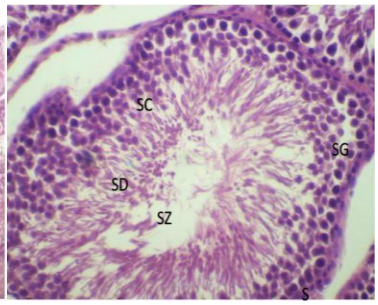

Figure (3) (x 400)

Testicular sections from rats treated with 1000 mg/kg of $K_2Cr_2O_7$ **(**Figures 3 and 4) displayed densely arranged seminiferous tubules accompanied by **i**nterstitial exudates and mild disorganization of the spermatogenic epithelium**.** The normal arrangement of spermatogenic cells was disrupted, with noticeable separation from the basement membrane **(**arrow). (H&E stain).

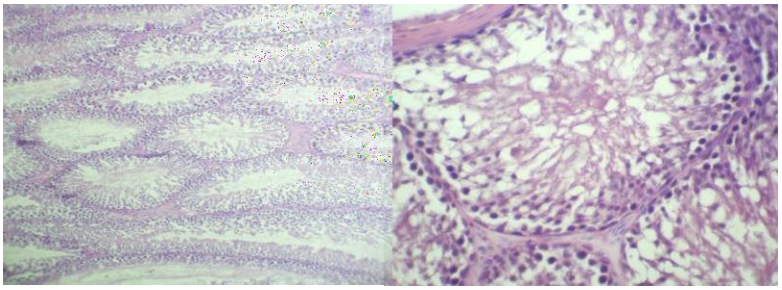

Figure (4) (x 200) **Figure (5) (x 400)**

Histological sections of testes from rats treated with 2000 mg/kg of $K_2Cr_2O_7$ (Figures 5 and 6) showed seminiferous tubules with pronounced separation (arrow) and severe disorganization of the spermatogenic epithelium. The tissue exhibited a significant reduction, detachment (arrow), displacement, and degeneration of spermatogenic cells (H&E stain).

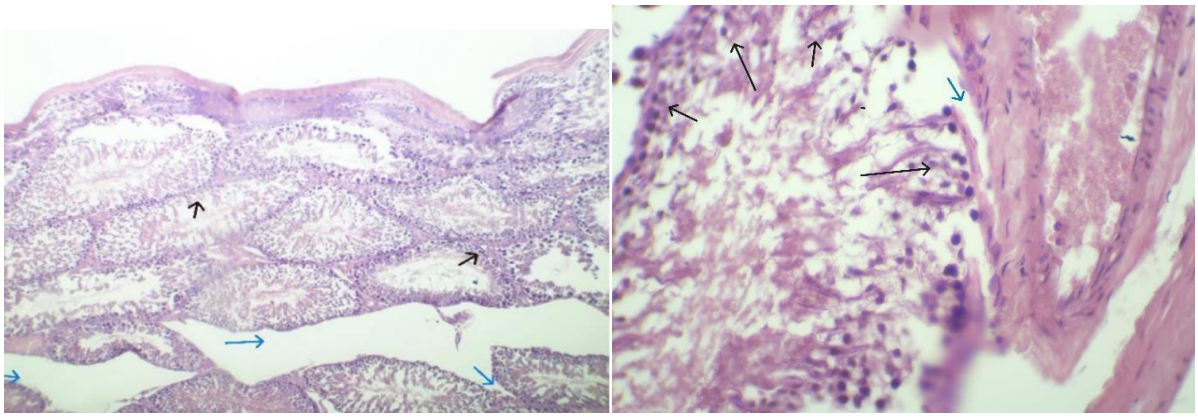

Figure (6) (x 200) **Figure (7) (x 400)**

Histological sections of liver tissue from the control group (Figure 7) displayed a normal architecture**,** with healthy hepatocytes and a typical central vein (H&E stain).

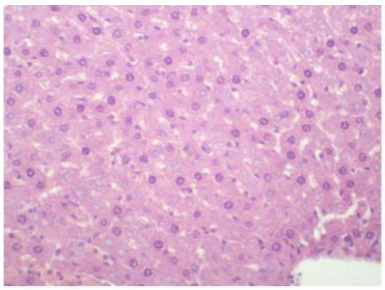

Figure (8) (x 400).

Histological examination of liver tissue from rats treated with 1000 mg/kg $K_2Cr_2O_7$ (Figure 8) revealed architectural disturbances, with numerous apoptotic and shrunken hepatocytes showing chromatin condensation **(**red arrows), alongside sinusoidal congestion with

erythrocytes (black arrow) (H&E stain).

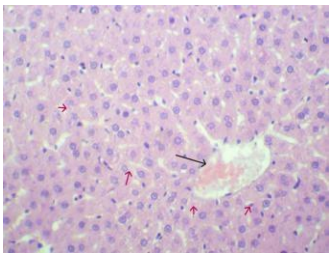

Figure (9) (x 400)

Liver sections from the group treated with 2000 mg/kg of $K_2Cr_2O_7$ (Figure 9) showed severe architectural damage**, i**ncluding hepatic vacuolation (black arrows), periportal hepatocyte necrosis (red arrows), and infiltration of mononuclear inflammatory cells (blue arrow) (H&E stain).

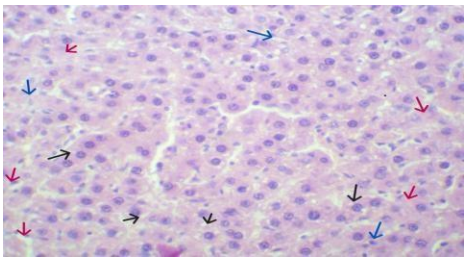

Figure (10) (x 400)

DISCUSSION

Evidence suggests that the widespread careless use of toxic heavy metals over the past two decades has raised serious concerns for male reproductive health. Testes are particularly vulnerable to metal-induced oxidative damage due to their high content of polyunsaturated membrane lipids.[28]

Exposure to hexavalent chromium compounds can cause degeneration in the outer layers of several seminiferous tubules, leading to a reduction in sperm count and spermatogonia per tubule and a significant increase in morphologically abnormal sperm. Similarly, oral administration of vanadyl sulfate for 60 days has been shown to reduce the weights of testes and accessory reproductive organs, decrease the diameter of seminiferous tubules, and shrink Leydig cell nuclei.[29]

The present study aimed to investigate the toxic effects of $K_2Cr_2O_7$ on the testes and liver of prepubertal male rats. Numerous studies have also documented toxic and carcinogenic effects

in humans and animals exposed to certain heavy metals. Extensive research has shown that metals such as iron, copper, cadmium, chromium, mercury, nickel, and vanadium can generate reactive oxygen species (ROS), leading to lipid peroxidation, protein depletion, and various other cellular damages. Potassium dichromate, a form of hexavalent chromium (Cr^{6+}), has been reported to cause toxicity related to oxidative stress in both humans and animals.[30] Upon exposure, potassium dichromate interacts with oxygen in the body, resulting in serious harmful effects such as allergic dermatitis, acute and chronic toxicity, neurotoxicity, dermatotoxicity, genotoxicity, carcinogenicity, and immunotoxicity.[31] Chromate ions (CrO_4^{2-}), which exist as neutral aqueous solutions of Cr(VI), are highly reactive and can penetrate cell membranes via nonionic anionic channels.[32] Numerous studies have further documented the tissue-damaging effects of different chromium compounds.[33,34]

Linos et al. (2011)[35] reported that long-term contamination of water sources with Cr(VI) for at least 20 years in the Oinofita region of Greece was associated with increased incidences of liver, lung, and kidney cancers. Hexavalent chromium compounds, including potassium dichromate ($K_2Cr_2O_7$), sodium chromate, and chromic acid, are extensively used in industries such as leather processing, electroplating, welding, chrome plating, and paints and coatings. The toxic effects of chromium can be detected through blood, urine, and tissue analyses of workers in these industries. Inhalation exposure may lead to lung and sinus cancers, while high-dose or accidental exposure can result in potentially fatal respiratory, cardiovascular, gastrointestinal, hepatic, renal, and neu- rological effects. Chromium exposure also negatively affects reproductive health and fetal devel- opment.[36]

A recent publication reassessed previous data and confirmed a link between Cr(VI) contamination and stomach cancer mortality.[37], although another study[38] using a different comparison group did not observe this association. To evaluate the carcinogenic potential of Cr(VI) via oral ingestion, the National Toxicology Program (NTP) conducted a 2-year study, demonstrating that Cr(VI) in- duced cancer in F344/N rats and B6C3F1 mice following oral exposure.[39,40] Besides carcino- genic effects, oral Cr(VI) exposure can also produce non-neoplastic lesions in rats and mice. In the current study, spermatogonia and primary spermatocytes in the control group were well organized, with spermatids and spermatozoa present, and Sertoli cells exhibiting large, pale nuclei along the basement membrane, representing normal testicular architecture. In the 1000 mg/kg treated group, mild disorganization was observed, with some spermatogenic cells losing their normal arrange-

ment and separating from the basement membrane, suggesting early testicular histological altera- tions.[41] In the 2000 mg/kg treated groups, there was severe detachment and disorganization of the spermatogenic epithelium, characterized by a marked reduction, displacement, detachment, and degeneration of spermatogenic cells, resulting in major disruption of testicular tissue architec- ture. In contrast, liver sections from the control group exhibited normal histology, with well-pre- served hepatocytes and a central vein showing no pathological changes.[42] Liver tissue from the 1000 mg/kg treated group showed mild tissue disruption, with many hepatocytes displaying apop- totic features, such as shrinkage and chromatin condensation. Sinusoidal congestion with red blood cells was also observed, indicating early signs of hepatic injury. In the 2000 mg/kg treated group, liver sections revealed more severe architectural damage, including hepatic vacuolation and peri- portal necrosis, along with mononuclear inflammatory cell infiltration, reflecting advanced liver injury and inflammation.

These results demonstrate that potassium dichromate is toxic to male reproductive tissue, causing disorganization and death of spermatogenic cells, and also induces hepatotoxic effects, including apoptosis, vacuolation, and inflammatory infiltration. These findings underscore the importance of investigating the adverse effects of hexavalent chromium compounds on reproductive and liver health. Further research is needed to elucidate the underlying mechanisms and to explore potential strategies to prevent or mitigate these pathological changes. These findings are consistent with previous studies[43] that described how cells rapidly take up hexavalent chromium and convert it to trivalent chromium within tissues. This observation also supports earlier research, such as the study by[44], which investigated the effects of environmental contaminants on lipid metabolism in male rats.

CONCLUSION

This study draws proper inferences about the toxic effect of potassium dichromate on the fertility pattern of the male rat. The histological alterations in testes as well as in liver tissues were dose- dependent, which illustrates the potential danger caused by exposure to hexavalent chromium through this compound. This showed the acute toxicity of potassium dichromate, which emphasizes that the compound should be handled carefully and needs proper disposal to avoid hazardous effects. Thus, findings of the current study are more supportive of previous results whereby hexavalent chromate elicited adverse effects on different biological systems, including reproductive organs. Furthermore, given that male

infertility currently represents a growing global health challenge, particular attention must be paid to the functions of various compounds, including potassium dichromate, in the development of intervention and control strategies. Long- term follow-up research into transgenerational effects and persistent fertility alterations shall be mandatory to assess the hexavalent chromium exposure risk fully. Indeed, investigations on the molecular mechanisms of potassium dichromate-induced reproductive toxicity should target oxidative stress, inflammation, as well as cellular-damage pathways. The study brings new knowledge to the field of environmental contaminants and their harmful effects on male fertility.

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