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The Testicular Toxicity Caused by 2, 3, 7, 8-tetrachloro-dibenzo-p-dioxin in \ Rats, as well as the Potential Protective Impact of Resveratrol

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Abstract

DURING the developmental stage, both humans and animals exhibit heightened sensitivity to exposure to harmful substances. Dioxin, being an endocrine disruptor, is recognized for its ability to affect testicular functioning and fertility. The current study sought to investigate the influence of Resveratrol (RES) on the harmful effects of 2, 3, 7, 8-tetrachloro-dibenzo-p-dioxin (TCDD) in the testicular tissue of rats. (Acute and subacute toxicity models were executed, where the experimental design was consisted of 7 groups ; G1 (control –ve), G2 vehicle (acetone + corn oil), G3 TCDD (4 µg/kg b. w.), G4 TCDD (2 µg/kg b. w.), G5 50 microgram/kg b w (RES), G6 (TCDD (4 µg/kg b. w.)+ RES),G (TCDD(4 µg/kg b. w.) + RES). The serum hormonal levels of testosterone were analyzed. The results of the current study demonstrate that the intoxication of TCDD leads to testicular injury, specifically affecting serum hormone levels and semen analysis parameters. Furthermore, assessment of the testis's microscopic features, including a histological defects due to. exposure to TCDD and the rise in apoptotic activity were detected. Furthermore, our findings unequivocally illustrate the therapeutic capacity of Res in mitigating testicular damage generated by TCDD.

Keywords: Resveratrol, TCDD, Sertoli cell, Sperm quality, Testicular damage.

Introduction

There are signs of a growing recognition of the potential impact of environmental pollutants on male reproductive health.[1]. Environmental contaminants can disrupt male reproductive function at different possible target organs. The testes are the most essential organ; responsible for sperm production and synthesis of testosterone, a male hormone [2]. The global concern regarding the impact of exposure to these persistent organic pollutants on the health of people has been significant. Various environmental toxicants have been demonstrated to have a detrimental impact on the process of spermatogenesis in both rodents and humans, resulting in reduced sperm count, aberrant sperm structure, and diminished semen quality [3]. 2, 3, 7, 8-tetrachloro-dibenzo-p-dioxin (TCDD) is a chemical compound that is produced as a product of different industrial processes including the production of chemicals and pesticides, incinerating household waste, causing forest fires, and engaging in the burning of waste. Dioxins are present in trace amounts worldwide, existing in the atmosphere, soil, water, sediment, as well as in many food sources including dairy products, meats, fish, and shellfish [4, 5]. Dioxins, which have a high degree of resistance to biodegradation, have endured in the environment for an extended period. These substances could accumulate in the adipose tissues of animals within the dietary cycle and is commonly found in breast milk. [6]. Reproductive toxicity, which can affect both males and females, is one of the potential toxicities associated with TCDD. Research has demonstrated that the testis is highly susceptible to the harmful effects of dioxin [7]. TCDD has detrimental effects on the male reproductive system, leading to a decrease in the size of the testes, prostate gland, and seminal vesicle. Additionally, it causes a reduction in sperm count and an increase in the quantity of abnormal sperm [8]. TCDD has been found to induce atrophy and damage to the testicles. A study has indicated that Sertoli cells in guinea pig testes may be affected by TCDD, resulting in

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alterations to the germ cells[9] TCDD exerts its harmful effects via attaching to the aryl hydrocarbon receptor (AhR)[10]. This mechanism, although not completely understood, results in changes in important biochemical and cellular processes, such as increased transcription of several genes that produce enzymes critical for drug metabolism and the activation of tyrosine kinases [11]. Activation of tyrosine kinase leads to disruptions in endocrine and paracrine signaling, as well as alterations in cellular processes, such as cell proliferation and development [12]. The AhR expressed in several organs throughout fetal development, such as the testis, indicating that these organs may have a higher vulnerability to TCDD [6]. The lack of an AhR during the development of male rodents resulted in alterations in both the absolute and relative weights of their testicles [13].

Resveratrol (RES; 3,5,4-trihydroxystilbene), a type of polyphenolic phytoalexin present in grapes and other seed-bearing plants, has been identified as a competitive antagonist of the AhR receptor in various types of cells. [14] that exhibits advantageous characteristics such as anti-carcinogenic and anti-tumor capabilities. [15], anti-hepatotoxicity [16], anti-nephrotoxic [17], anti–inflammatory [18], anti-depressive, antioxidant [19, 20, 21] and the effects of enhancing immunity [22]. RES functions as a preventive agent against damage caused by aryl hydrocarbon [23]. Supplementation of resveratrol to adult rats led to increased sperm production and higher levels of testosterone in the bloodstream, suggesting beneficial effects on the male reproductive system. An independent investigation showed that the application of resveratrol to mature rats led to improved movement of sperm and prevention of the oxidation of lipids forming lipid peroxides [24]. The aim of this study was to evaluate the influence of resveratrol on the damage caused by TCDD on the male reproductive system in rats, taking into account the toxic effects of TCDD and the mechanism of action of resveratrol

Material and Methods

Animals

One hundred and two male Wistar rats were supplied from the Animal House at the Faculty of Veterinary Medicine, Tikrit University. The rats were of age 8-9 weeks and a weight ranging from 80-90 grams. All experimental protocols and experimentation on animals' subjects were approved by animal ethics commission (687/P.G./2024). The rats were housed in a regulated environment maintained at a temperature of 25 °C and a humidity level ranging from 55 to 60%. They experienced a 12-hour period of light followed by a 12-hour period of darkness. The rats were given a standard pellet diet and had unlimited access to water. Drinking water was replenished every day, while the animal enclosure was cleaned every alternate day.

Chemical preparation

The 2,3,7,8-TCDD (purity>99%) was supplied from Accustandart, Inc. (New Haven, Connecticut, USA). The TCDD dose was prepared by dissolving 1mg of TCDD in acetone, followed by mixing it with corn oil. Resveratrol was obtained from ark pharm USA. Resveratrol was prepared by dissolving in distal water with overtaxing. Rats, under investigation, were divided into three groups and the experimental protocol was held for 100 days

Acute toxicity (Dixon method, 1980s):

The determination of TCDD LD50 utilized the up-and-down method [25], employing a dose range of 20-80 µg/kg of TCDD as outlined by Pohjanvirta and Tuomisto,[26]. Thirty-two rats were allocated LD_{50} for this investigation, with four assigned to each dose level. Doses were adjusted by either increasing or decreasing by 100% of the initial dose based on the survival or mortality of the dosed rat after 21 days. The median lethal dose was computed based on the mortality of 50% of the animals.

Chronic toxicity

First group (C -ve)

Control group including (10) rats were fed on ordinary rat pellets and water ad libitum.

Second group (C +ve)

(10 rats) were administered orally by gavage 1 ml from vehicle (acetone + corn oil) solution weakly for 100 days.

Third group (10%)

(10 rats) were administered orally by gavage 1/10 from LD_{50} TCDD dissolved by acetone + corn oil solution weekly for 100 days.

Fourth group (5%) :(10 rats) were administered orally by gavage 1/20 from LD50 TCDD dissolved by acetone + corn oil solution weekly for 100 days.

Fifth group (Resveratrol): (10 rats) were administered orally by gavage 50 microgram Resveratrol dissolved by Distal water weekly for 100 days.

Sixth group (10% from LD_{50} of TCDD + Resveratrol): (10 rats) were administered orally by gavage 10% from LD50 TCDD dissolved by acetone + corn oil solution+ 50 microgram Resveratrol dissolved by Distal water weekly for 100 days.

Seventh group (5% from LD_{50} of TCDD + Resveratrol): (10 rats) were administered orally by gavage 5% from LD50 TCDD dissolved by acetone + corn oil solution + 50 microgram Resveratrol dissolved by distal water weekly for 100 days.

TCDD was orally administered at a dosage of LD50 in acute toxicity experiments. For chronic toxicity studies, TCDD was orally administered at dosages of 1/10 and 1/20 of the LD50 dose µg/kg/week [27]

Blood collection: Blood were collected at day 100 of the experiment according to the collection protocol [28], for serum testosterone assay Were measured by rat ELISA kit Clone- Corp USA [29].

Histopathological changes: At the end of experiment (100) days all animal were scarified under slight ether anaesthesia and testis swiftly extracted and dissected to note any abnormalities in size, colour, consistency, or adherence. Subsequently embedded in paraffin and stained using a standard stain (hematoxylin and eosin) after being fixed in 10% formalin, thrown in ascending grades of ethanol (70, 80, 90, 100%), and then thrown in xylene [28, 30].

Evaluation of sperm characteristics

The semen collected and sperm motility, viability, count and abnormality were evaluated according to [31].

Statistical analysis

Data analysis by using computer statistical program SPSS and sigma stat program. Tow way analysis variance was used $p \leq 0.05$ [6].

Results

Median lethal dose of TCDD

The results revealed that the LD_{50} of TCDD was 40 µg/kg, B.W. LD_{50} of TCDD was 40 µg/kg B.W. that killed half of the animals in single dose orally. The findings are consistent with Simanainen *et al*. [31].

Serum hormonal profiles of testosterone

Results in Fig. (1) indicated that the testosterone hormones concentration significantly decreased mean ± SE ($P < 0.05$) in 3rd group (TCDD 10%) 4th group (TCDD 5%) compared with control group, while testosterone hormones significant increased mean ± SE ($P < 0.05$) in 5th group (resveratrol).

Semen evaluation

Sperm count

Investigation of the semen sample from the 3rd group (TCDD 10%) and 4th (TCDD 5%) revealed a statistically significant drop ($P \leq 0.05$) in the mean total semen, sperm count, and active sperm characteristics as compared to the control group, while significant increased mean ± SE($P \leq 0.05$) in 5th group (resveratrol) see the below Fig.(2).

Sperm motility

Results showed a significant motility reduction in the all-administrated groups except 5th group. On the other hand, the 3rd group (TCDD 10%) and 4th (TCDD 5%) sperm motility values were significantly ($p \leq 0.05$) lower than the control groups' values for high, moderate, and slow motility. Furthermore, a significant decrease in motility values was observed in the groups that were administered varying dosages of TCDD, in comparison to the groups that were not administered. The 5th group exhibited a greater quantity of aberrant, irregular, and deformed sperms compared to the 3rd and control groups. The rates of aberrant sperm showed a proportionate rise when TCDD was supplied with drinking water (Fig. 3).

Sperm viability

The Fig. (4) indicates a statistically significant ($p \leq 0.05$) decline in linearity, straight rectilinear movement, wobbling, beating cilia frequency, and number of sperm in rectilinear movement in the 3rd group (TCDD 10%) and 4th (TCDD 5%) compared to the control groups.

Sperm abnormality

Examination of sperm abnormality of the 3rd group (TCDD 10%), 4th(TCDD 5%) revealed a significant increase at ($P \leq 0.05$) in the parameters of mean total semen, sperm count and active sperm in comparison with these of control group, while significant decreased mean±SE in 5th group (resveratrol) see the below Fig. (5)

Histopathology

G3: edema vacuolation in the width interstitial layer with decease .in Leydig and germ cells. Seminiferous tubules degenerated and atrophied with many multinucleated giant cells in the lumen of degenerated seminal tubules formed by fusion of degenerated spermatogenic cells Fig.(6). Sever interstitial hemorrhage with vacuolated seminal tubules (without spermatogenesis) and decrease in Sertoli cells, increase in the fibrous connective tissue the interstitial layer with spermatic cells (spermatocytes) apoptosis Fig.(7). Part of the wall of seminiferous tubule showed characteristic foamy cytoplasmic appearance of lipid containing tissue Sertoli cells necrotic with oedema surrounded , increase thickening of seminiferous wall by fibrous connective tissue, apoptotic cells Fig. (8).

The G 4 all blood vessels dilated on congested with sever edema in the interstitial layer atrophied and decrease in leydig and germ cells with most seminiferous tubules atrophied and Sertoli cells separated necrosis Fig. (9) apoptotic Sertoli calls with accumulating le the central tubule with adhesive together of sertolie thicken Seminiferous tubules wall Fig.(10) and multinucleated degenerated Sertoli cells Fig. (11). Thick tunica albuginea layer

(connective tissue and smooth muscle) with decrease in interstitial tissue and leydig cell , decrease in the interstitial (intertubules) tissue space Fig. (12).

In G5, Testis showed normal seminiferous tubules, congested blood vessels Fig.(13) while G6 interstitial layer edema with mild seminiferous tubules degeneration Fig.(14). G7 showed normal seminiferous tubules Fig. (15).

Discussion

The toxicity of reproduction has garnered growing attention and apprehension in recent years [33]. Environmental pollutants recognized to cause severe toxicity to all body systems [34] For example, disrupting the balance between prooxidants and antioxidants can lead to oxidative stress, affecting reproductive functions [35]. TCDD is an environmental pollutant that has proven to cause reproductive problems in both wildlife and humans by reducing fertility [1]. The current investigation observed a decrease in serum testosterone levels, which suggests an overproduction of reactive oxygen species (ROS) and the initiation of oxidative stress (**Figure 1**). The decrease in testosterone levels reported after exposure to TCDD may attributed to the detrimental impact on Leydig cells. Furthermore, TCDD has suppressive effects on the release of luteinizing hormone (LH) from the pituitary gland [36]. Primary cultivated Leydig cells have shown oxidative alterations after being exposed to 2-bromopropane, an intermediate compound utilised in pesticide manufacturing, as well as cadmium. This exposure led to a reduction in the release of testosterone [37] upon administering a solitary injection of TCDD into the peritoneal cavity of adult male rats, a reduction in the dimensions of Leydig cells in the testes was observed. These findings indicate that Leydig cells are vulnerable to the detrimental impacts of TCDD [38]. Studies have demonstrated that TCDD can hinder the release of testosterone caused by human chorionic gonadotropin (hCG) in primary cultures of rat Leydig cells. This is achieved by reducing the activity of steroiodogenic enzymes (StAR, P450scc, and 3β-hydroxysteroid dehydrogenase) and the concentration of cAMP within the cells [9]. TCDD exhibits antiandrogenic properties in both humans and animals, potentially impacting the structure and functionality of the testes [39]. TCDD suppressed the seminal vesicle epithelium undergoes expansion and differentiation during postpartum growth and development, leading to atrophy and reductions in the circumference of the seminiferous tubules and the population of spermatogonia [40]. A study in epidemiological revealed a negative association between testosterone levels and serum TCDD. Additionally, men who were persistently exposed to TCDD experienced a 50% drop in the number of spermatozoa compared to normal levels [41]. Our analysis revealed that TCDD caused a decrease in both the number and movement of spermatozoa, while also increasing the proportion of non-viable and deformed sperm. The findings suggest structural damage to the testis in rats, as depicted in **Fig.** (**2-5**).

TCDD exerts its detrimental effects primarily by attaching to the AhR, which then forms a complex with another protein known as aryl hydrocarbon receptor nuclear translocator. This intricate structure subsequently binds to specific sections in the DNA of target genes, referred to as response elements, and controls the expression of these genes [42]. The activation of AhR stimulates the production of several genes containing enhancer regions contain xenobiotic responsive elements. An instance is the gene accountable for cytochrome P450[43]. The potential cause of the testosterone drop could be attributed to TCDD's ability to harm the smooth endoplasmic reticulum or mitochondria of the Leydig cells, which in turn disrupts the functioning of enzymes responsible for androgen production [44].

Exposure to TCDD can lead to changes in the structure of the testicles and a reduction in the production of steroids [1]. Similarly, in this experiment, the administration of TCDD led to changes in the physical structure. The seminiferous tubules, comprising predominantly Sertoli cells and a limited population of germ cells, exhibited necrotic and severely damaged characteristics. Thus, the presence of TCDD in the testicles led to abnormal sperm production. There is a notable concern exposure to environmental pollutants can have substantial pathogenic impacts on the genital systems of humans as well as animals. TCDD is currently recognized as the most powerful environmental toxin known, and scientific evidence has shown that it can lead to reproductive issues [45]. The present study revealed histopathological alterations within the tubules of seminiferous tissue within the testis, spanning from blood vessel congestion to diffusely spread interstitial edema. After delivering dioxin to the experimental rats, we detected specific areas of tubular degeneration and necrosis. Additionally, the interstitial tissue in the treated rats exhibited a notable increase in interstitial edema and congested blood vessels, indicating the presence of inflammation. Furthermore, there were indications of apoptosis in Leydig cells. Subsequently, the seminiferous tubules were found to be spaced apart from each other, with evidence of deteriorated peritubular tissue interspersed. Consistent with the current findings, TCDD was observed to induce The experimental animals had atrophied testis with significant morphological changes, reduced spermatogenesis, and lesions in the epididymis[46].

In addition, the administration of TCDD on rats resulted in histopathologic changes showing a reduction in the size of seminiferous tubules and the quantity of testicular sperm [44]. Antioxidants are

molecules that can be either derived from external sources or produced within the body. They function in many ways, such as removing reactive oxygen species (ROS) or their precursors, preventing the development of ROS, and binding metal ions that are necessary to produce ROS [47,48]. Flavonoids have the capacity to counteract ROS, such as hydroxyl radical and superoxide anion, therefore reducing oxidative damage [49]. The antioxidant effects of flavonoids are determined by their ability to both bind to metals and scavenge reactive oxygen species, which are free radicals. RES, short for resveratrol, is a dietary flavonoid that is extensively researched. It can be found in several sources such as vegetables, fruits, and other foods [50]. RES, a powerful antioxidant, directly neutralizes free radicals, prevents lipid peroxidation, and modifies the antioxidant defense system [51, 52]. The protective effects of RES on the metabolism of antioxidant enzymes and histological alterations in rat lung tissues induced by chlorpyrifos [53]. The results of our study unequivocally demonstrated that treatment with RES effectively averted oxidative and histological damage induced by TCDD. Nevertheless, our findings in the current study encompassed biochemical indicators related to harm to the testicles, such as measurements of testosterone levels. However, it was suggested that combining RES therapy with TCDD could reduce the negative consequences of TCDD in terms of histological changes. The administration of RES therapy demonstrates strong protective benefits against histological damage induced by many chemicals, including cadmium [54], paracetamol [55] and ethanol [56]. The positive impacts of RES on the testicular toxicity of TCDD are attributed to its significant antioxidant ability [57].

Conclusion

The present investigation revealed that exposure to TCDD resulted in a decline in semen quality. Furthermore, there was a drop in testosterone levels and several histological alterations were observed in the testis. The results of our investigation show that the administration of RES alongside TCDD considerably decreases testis toxicity in rats, showing a potent ameliorative effect of this flavonoid. Therefore, the objective of this study was to elucidate the therapeutic advantages of RES when co-administered with TCDD in order to mitigate its detrimental impact on reproductive function.

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Funding statement

The authors declare that the present study hasno financial issues to disclose.

Conflict of interest

The authors declares that there is no conflict interest.

Author's contributions

Ahmed A. Sultan: Research article, funding the acquisition and preparing materials and review. Bushra. I. al. Kaisi: Explain the finding, Experiment design, statistical analysis and editing.

Ethical approval

It was granted through the local committee of the animal care and use at the College of Veterinary Medicine/University of Baghdad (Number 687/P.G. at 27/3/2024).

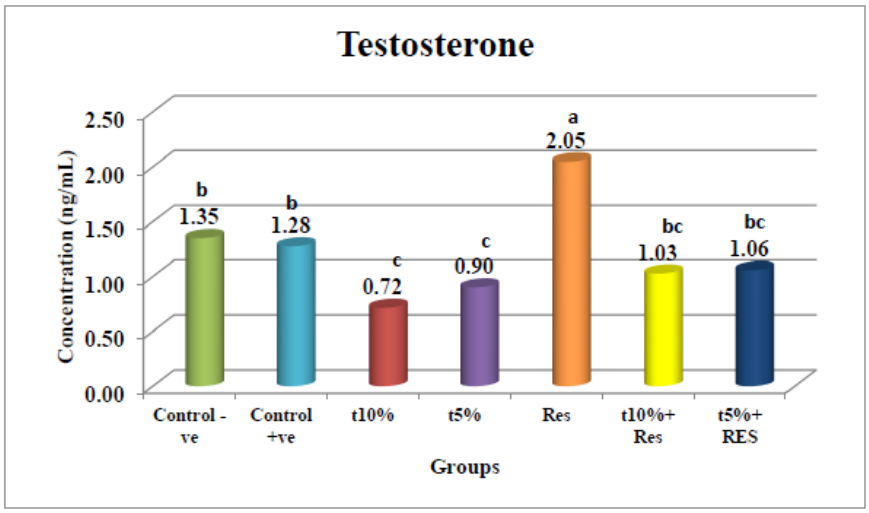

Fig. 1. Effect of TCDD on testosterone hormones (ng/mL) in serum of Wister male rats

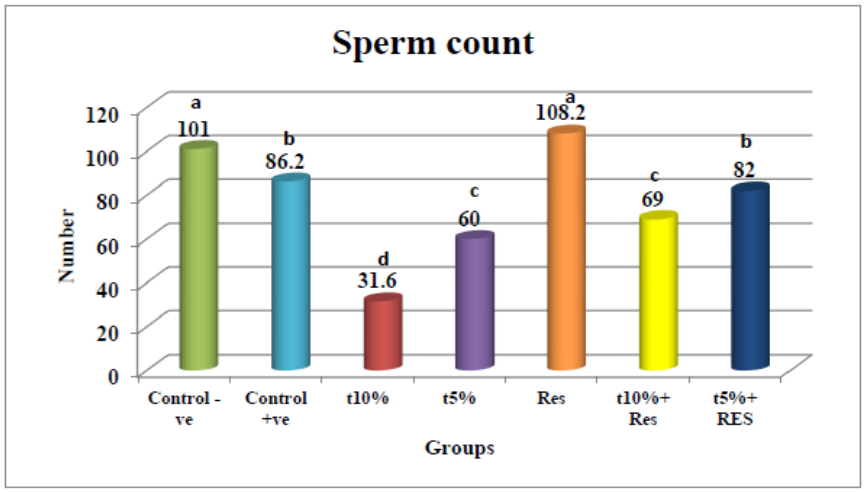

Fig. 2. Effect of TCDD on sperm count of albino male rats. The different letters indicated that the present of significant differences among groups. The same letters indicated that non-significant differences among the groups.

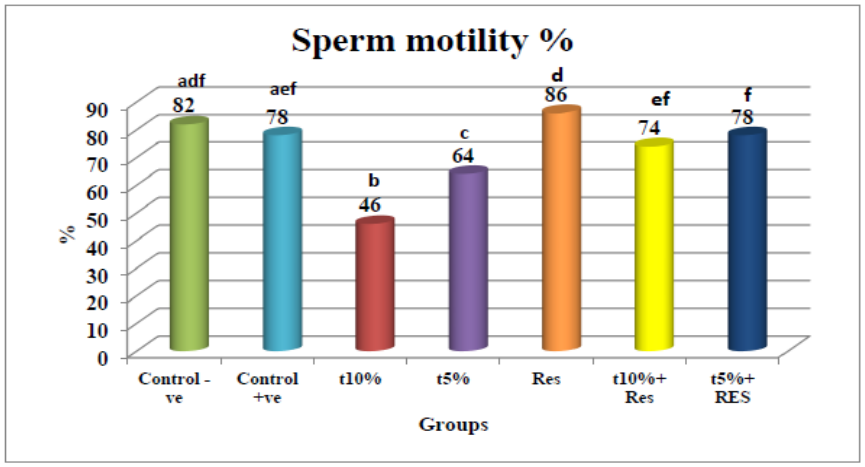

Fig. 3. Effect of TCDD on sperm motility of albino male rats. The different letters indicated that the present of significant differences among groups.

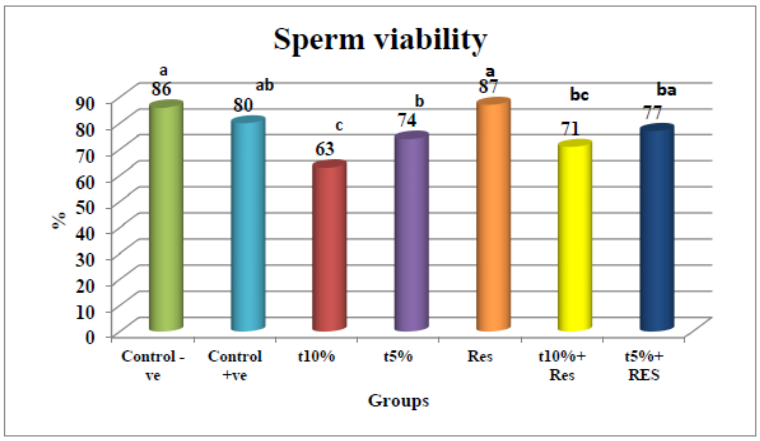

Fig. 4. Effect of TCDD on sperm viability of albino male rats. The different letters indicated that the present of significant differences among groups.The same litters indicated that non-significant differences among the groups.

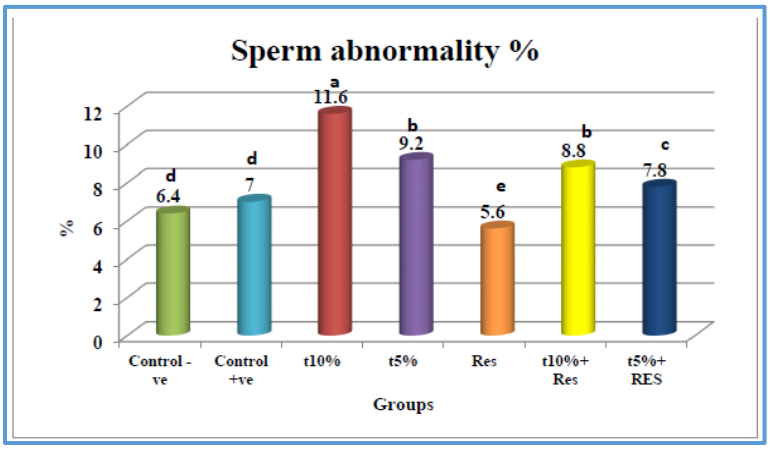

Fig. 5. Effect of TCDD on sperm abnormality of albino male rats. The different letters indicated that the present of significant differences among groups. The same letters indicated that non-significant differences among the groups.

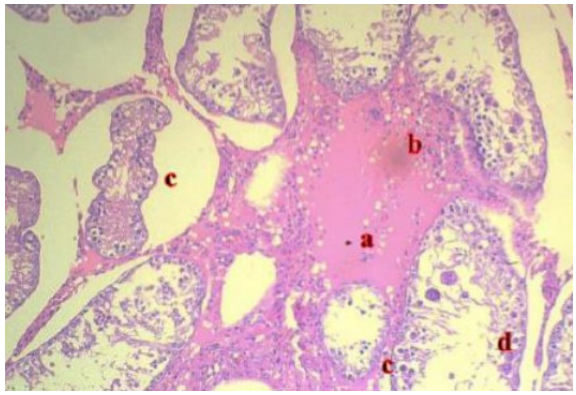

Fig. 6. A micrograph of part of the rat testis of G3 (10 % LD_{50} TCDD) showed a) edema and vacuolation in the width interstitial layer b) decrease the Leydig and germ cells c) degenerated and atrophied of seminiferous tubules d) Many multinucleated giant cells in the lumen of the seminiferous tubules, formed by fusion of degenerated. spermatogenic cells. X400 HandE stain.

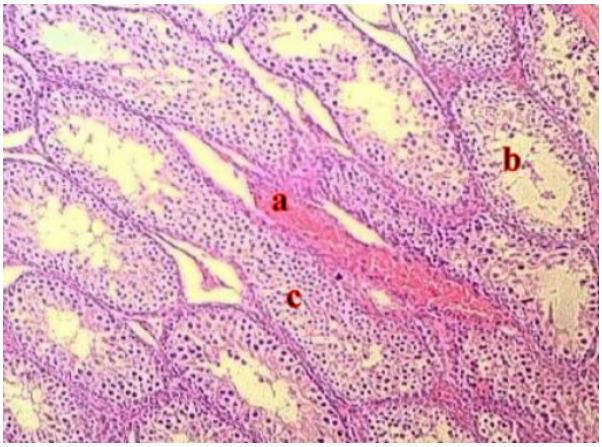

Fig. 7. A micrograph of part of the rat testis of G3 (10 % LD50 TCDD) showed a) Sever Interstitial hemorrhage b) all seminiferous tubules vacuolated without spermatogenesis and decrease in the sertoli cells c0 increase in the fibrous connective tissue in interstitial layer between tubules c) apoptotic cells in the spermatic cells. X400 HandE stain

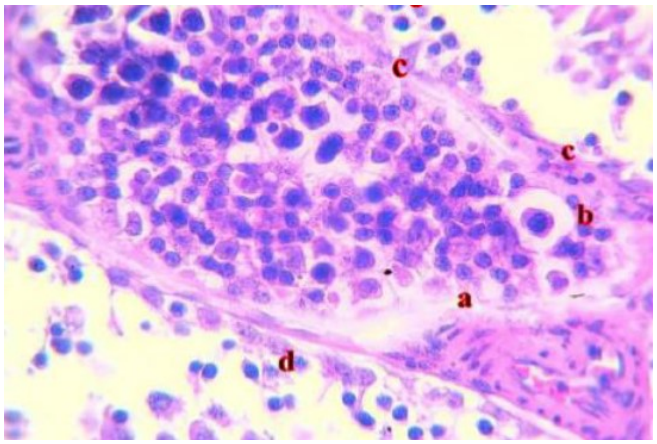

Fig. 8. A micrograph of part of the rat testis of G3 (10 % LD_{50} TCDD) showed a) part of the wall of seminiferous lobules showing Characteristic foamy cytoplasmic appearance of lipid-containing tissue b) Sertoli cell necrotic and edema surrounded c) Increase in the thickening of the somniferous wall by fiber connective tissue d) apoptotic cells. X400 HandE stain

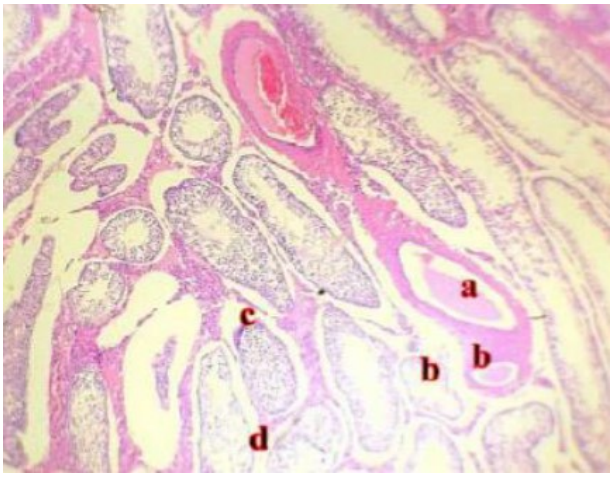

Fig. 9. A micrograph of part of the rat testis of G4 (5 % LD_{50} TCDD) showed a) all blood vessels dilated and congested b) atrophied and decrease in Leydig and germ cell c) Most of seminiferous tubules atrophied with Sertoli and spermatid cell necrotic. X200

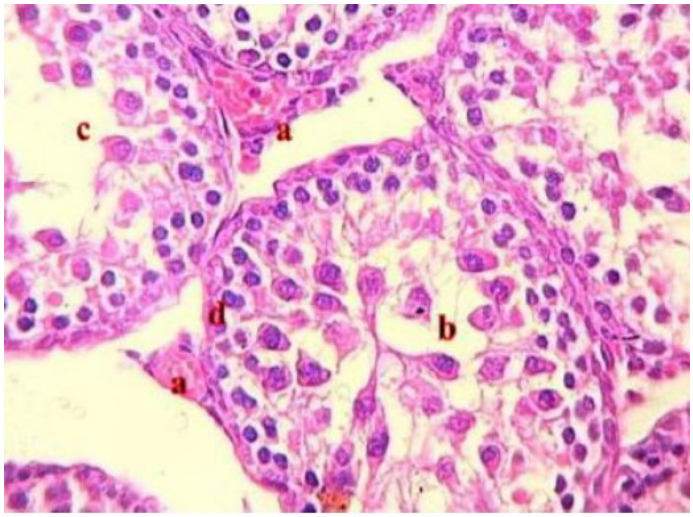

Fig. 10. A micrograph of part of the rat testis of G4 (5 % LD_{50} TCDD) showed a) congested blood vessels in the interstitial layer b) accumulation of adhesive necrotic Sertoli cells in the center of seminiferous tubule c) apoptotic of Sertoli cells d) thicken in the seminiferous tubule wall X400 HandE stain.

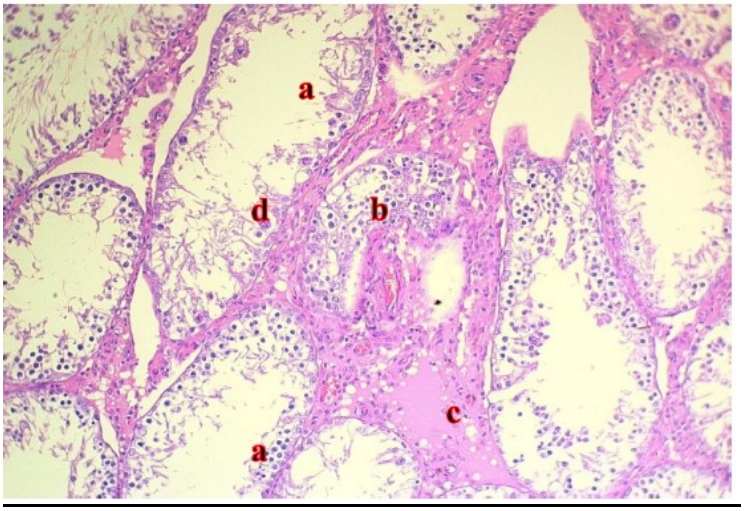

Fig.11. A micrograph of part of the rat testis of G4 (5 % LD50 TCDD) showed a) degenerated seminiferous tubules b) apoptotic of Sertoli cells in seminiferous tubules c) interstitial edema d) multinucleated degenerated Sertoli cells X400 H&E stain

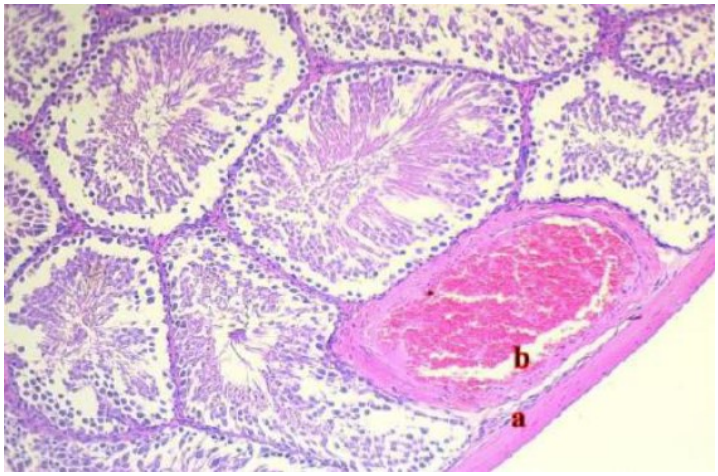

Fig. 12. A micrograph of part of the rat testis of G4 (5 % LD_{50} TCDD) showed a) thick in tunica albuginea layer (connective tissue smooth muscle) b) decrease in the interstitial (intertubular) tissue space c) decrease in inters interstitial tissue and Leydig cells X400 HandE stain

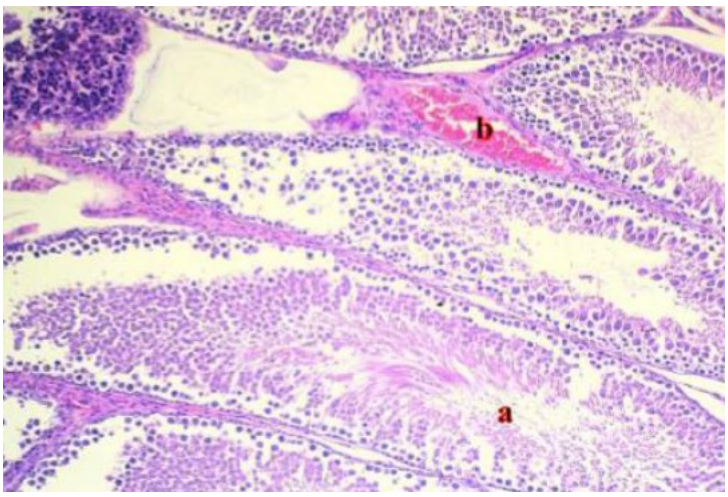

Fig.13. A micrograph of part of the rat testis of G5 (Resveratrol) showed a) normal seminiferous tubules b) congested blood vessels X400 H and E stain

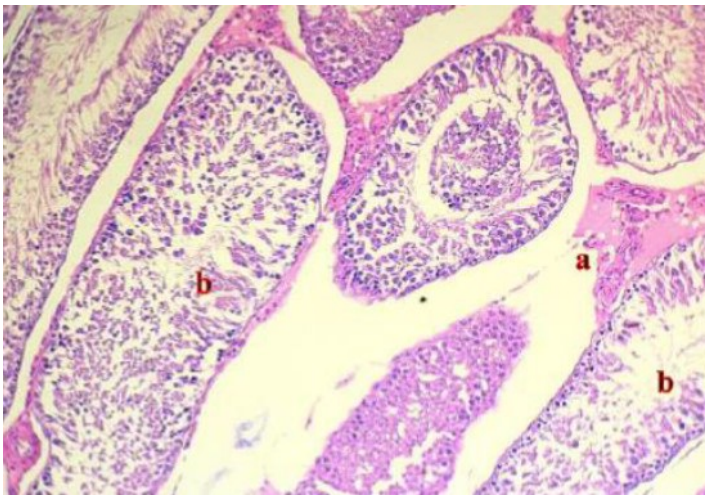

Fig.14. A micrograph of part of the rat testis of G6 (10 % LD_{50} TCDD + Resveratrol) showed a) Interstitial layer edema b) mild seminiferous degenerating X400 Hand E stain

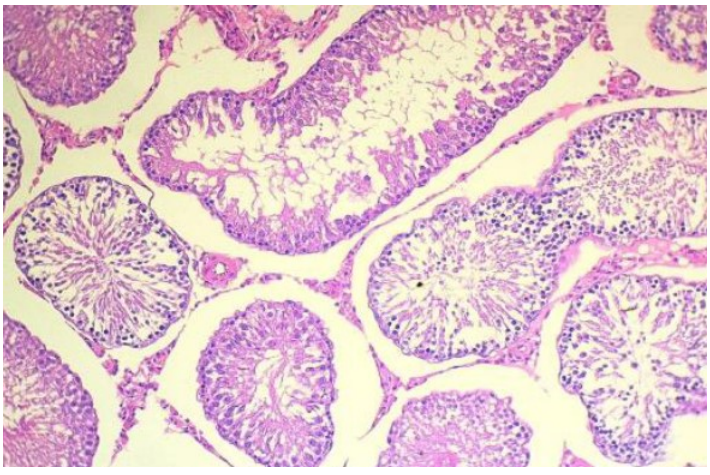

Fig.15. A micrograph of part of the rat testis of G7 (5 % LD_{50} TCDD + Resveratrol) showed a) normal seminiferous tubules (X400 H and E stain).

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سمية الخصية الناجمة عن 2، 3، 7، 8-رباعي كلورو ثنائي بنزو بي ديوكسين في الجرذان، بالإضافة إلى التأثير الوقائي المحتمل للريسفيراترول

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الخلاصة

خلال مرحلة النمو، يُظهر كل من البشر والحيوانات حساسية عالية للتعرض للمواد الضارة. الديوكسين، كونه مسببًا لاختلال الغدد الصماء، معروف بقدرته على التأثير على أداء الخصية والخصوبة. سعت الدراسة الحالية إلى دراسة تأثير RES على التأثيرات الضارة لـ TCDD في أنسجة الخصية لدى الفئران. تم تطبيقه على ذكور الجرذان البيضاء (102) فئران عمرية (8-9) أسابيع ونطاق الوزن (80 -90) جرام، تم استخدام (32) فأراً للمرحلة الحادة من التسمم، في حين تم استخدام (70) فأراً أخرى كـ سمية مزمنة. يتكون تصميم التجربة من 7 مجموعات ؛ 1G (التحكم –ve)، مركبة 2G (الأسيتون + زيت الذرة)، G3 TCDD (4 ميكروجرام/كجم من وزن الجسم)، G4 TCDD (2 ميكروجرام/كجم من وزن الجسم)، G5 (RES) (4 ميكروجرام/كجم من وزن الجسم)، G6 (TCDD،G5 (RES)، G5 (RES)، G6 (TCDD (4 ميكروجرام/كجم من وزن الجسم).)+ (TCDD،RES) G (4 ميكروغرام/كغ وزن الجسم) + RES). تم توثيق مستويات هرمون التستوستيرون في الدم. تظهر نتائج دراستنا أن تناول عقار TCDD يؤدي إلى إصابة الخصية، مما يؤثر بشكل خاص على مستويات هرمون المصل ومعلمات الحيوانات المنوية. وعلاوة على ذلك، تم إجراء تقييم على الهياكل المجهرية للخصية، بما في ذلك التحليل النسيجي. يؤدي التعرض لـ TCDD إلى تغيرات نسيجية في خصية الجرذان، مثل انحطاط الأنابيب المنوية، والنخر الأنبوبي، والتفريغ داخل الأنبوب، واتساع التجويف، والتشكيل غير الطبيعي للخلايا الجرثومية. تم اكتشاف ارتفاع واضح في نشاط موت الخلايا المبرمج. علاوة على ذلك، توضح النتائج التي توصلنا إليها بشكل لا لبس فيه القدرة العلاجية للريسفيراترول في تخفيف ضرر الخصية الناتج عن TCDD.

الكلمات المفتاحية: ريسفيراترول، TCDD، خلية سيرتولي، جودة الحيوانات المنوية، تلف الخصية.