# The Effect of Lead Acetate-Induced Oxidative Toxicity on Testicular Tissue in Male Rats, and the Protective Role of dried Apricot Fruit Extract and DHEA Treatment

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**Abstract**

This research was designed to determine the protective role of dehydroepiandrosterone (DHEA) and dried apricot fruit extract in reducing the toxicity of lead acetate to male fertility.

The study lasted for 35 consecutive days and included 35 male Sprague Dawley albino rats, aged between 6 and 7 months and weighing between 190 and 220 grams. The mice were divided into 7 groups, each group containing 5 rats. The study also showed a decrease in the concentration of 8-hydroxy-2′-deoxyguanosine (8-OHdG), and testosterone, sperm-stimulating hormone (SSH), and interstitial cell-stimulating hormone (ICSH) as a result of lead acetate treatment. Furthermore, the study indicated that lead acetate treatment led to histological changes in the testis, including damage to the basement membrane of the seminiferous tubule, damage to the interstitial tissue, degeneration and atrophy of Leydig cells, and a decrease in sperm production.

The results showed that treating rats with dried apricot fruit extract and DHEA treatment led to an increase in the activity of antioxidants (SOD, GPx , CAT) and a decrease in oxidative stress products OHdG-8 compared to the oxidative stress group, and a significant improvement in testosterone, ICSH, and SSH levels. With the observation of mature sperm in the seminiferous tubule lumen, Leydig cells in the interstitial tissue appeared to maintain their normal shape and structure, and spermatogenesis showed marked improvement, with a higher percentage of sperm and a greater number of sperm with straight, normal tails, With greater regularity in tail length and clearer connection between head and tail in most sperm.

**Keywords:** Dehydroepiandrosterone , Oxidative stress, Lead acetate, , Dried apricot fruit extract.

## Introduction

Heavy metals are a major cause of serious global public health problems in the environment. Lead and cadmium are among the most widespread toxic pollutants. These heavy metals occur naturally and are widely used in the manufacture of paints, batteries, and other products. Their accumulation in the environment poses a significant health risk if absorbed by humans and animals. [1]. One of the toxic properties of pollutants, including lead, is that it stimulates oxidative stress, which is one of the main causes of cell damage in various organs, such as the kidneys, liver, reproductive organs, and the brain [2]. The male reproductive system is one of the most sensitive bodily systems to oxidation, because sperm membranes are rich in unsaturated fatty acids, and because spermatogenesis is a very complex process that requires hormonal differentiation and regulation [3].

The imbalance between the production of reactive oxygen species (ROS) and antioxidant defenses is what causes the occurrence of oxidative stress. Reports have indicated that lead increases the production of ROS, leading to damage to cells and molecules, reduces internal antioxidants, and impairs enzyme functions, resulting in lipid peroxidation, DNA damage, and protein oxidation. [4]. Oxidative stress in the testes leads to impaired spermatogenesis, degeneration of seminiferous tubules, Leydig cell dysfunction, and germ cell death. Consequently, numerous studies have reported decreased sperm count, altered sperm morphology and motility, and significant changes in testosterone (T) levels, as well as in interstitial cell-stimulating hormone (ICSH) and spermatogenesis (SSH) levels following lead exposure. This oxidative stress effect from lead exposure may ultimately impact male fertility. [5,6].

In addition to medical treatment, recent studies have shown that healthy nutrition and dietary supplements can play an important role in improving male fertility. Many studies have confirmed that a diet consisting of a high percentage of fruits may reduce the risk of chronic diseases such as cancer, inflammatory diseases, infertility and other serious illnesses. Fruits possess vital and functional properties that exhibit important biological activities, such as phenolic acids, tannins, phenols and flavonoids [7,8].

In recent years, interest in nutritional supplements has increased, as they are among the most widely used products in the health field. They are used to support nutritional balance and improve physical performance. These supplements include a wide range of substances, such as vitamins, minerals, amino acids, as well as natural hormones and their derivatives. Interest has increased in studying their effect on reproductive functions and fertility, given their potential role in promoting hormonal balance and improving the quality of reproductive cells [9] .

Among the hormone supplements that have received increasing attention is Dehydroepiandrosterone (DHEA), a steroid hormone that is naturally secreted from the adrenal cortex and is a precursor to the formation of male sex

hormones such as testosterone. DHEA is considered one of the most important hormones supporting the maintenance of hormonal balance within the body, as its levels begin to rise in puberty to peak in the third decade of life, then gradually decline with age. Therefore, this hormone is used as a dietary supplement to compensate for age-related deficiencies or androgen deficiency [10] .

## 2. Materials and Methods

### 2.1 Experimental Animals

The study was conducted at the animal house of the College of Veterinary Medicine / Tikrit University and lasted for thirty-five consecutive days. It included thirty-five albino male rats of the Sprague Dawley breed, aged six to seven months and weighing between (190-220) grams. They were distributed in plastic cages into seven groups, with (5) animals in each group.

### 2.2 Experimental Design and Grouping

The animals within each group were selected to be of similar weights. The groups were arranged as follows: **Control group:** This group received distilled water and a standard diet daily for 35 days. **Lead acetate:** This group was administered lead acetate at a dose of 50 mg/kg body weight orally for 35 days. **Lead acetate group treated with DHEA:** This group received lead acetate at a dose of 50 mg/kg body weight orally, followed after 30 minutes by oral administration of DHEA at a dose of 4 mg/kg body weight. Treatment continued daily for 35 days . **Lead acetate group treated with dried apricot fruit extract:** This group was administered lead acetate at a dose of 50 mg/kg body weight orally, followed after 30 minutes by oral administration of dried apricot fruit extract at a dose of 1.5 mL/animal daily for 35 days. **Lead acetate group treated with dried apricot fruit extract and DHEA:** This group received lead acetate at a dose of 50 mg/kg body weight orally, followed after 30 minutes by oral administration of DHEA at a dose of 4 mg/kg body weight and dried apricot fruit extract at a dose of 1.5 mL/animal daily throughout the experimental period . **Dried apricot fruit extract–treated group:** This group received dried apricot fruit extract orally at a dose of 1.5 mL/animal daily throughout the experimental period **DHEA-treated group:** This group was administered DHEA orally at a dose of 4 mg/kg body weight daily throughout the experimental period.

### 2.3 Histopathological Examination

After the end of the experimental period, the testicles were removed from the animals after dissection, preserved in 10% formalin, then treated with paraffin and cut into 5 micrometer-thick sections. They were stained with hematoxylin and eosin (H&E) stain and examined under a light microscope.

### 2.4 Statistical Analysis

All values are presented as means ± standard error. One-way analysis of variance (ANOVA) was used for comparisons between different groups, with the difference considered statistically significant when the p-value was less than or equal to 0.05.

## 3. Results

### 3.1 -Histopathological Findings

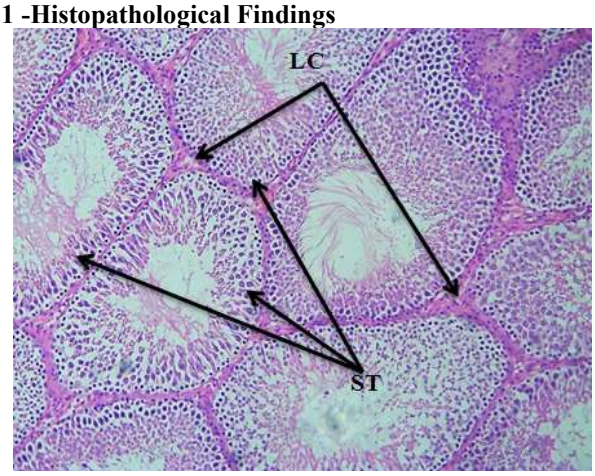


Image 1: Testicular section of the control group showing seminiferous tubules (ST) with normal structure. Leydig cells (LC) are clearly visible. H&E, 100×.

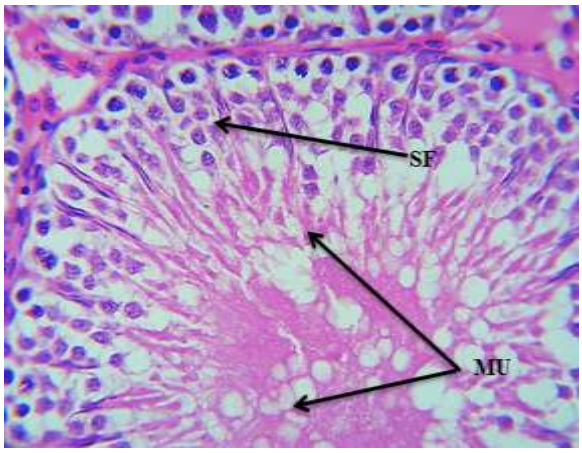


Image 2: Testicular section of the lead acetate-treated group showing accumulation of dense material within seminiferous tubules (MU) and unclear spermatogenesis (SF). H&E, 400×.

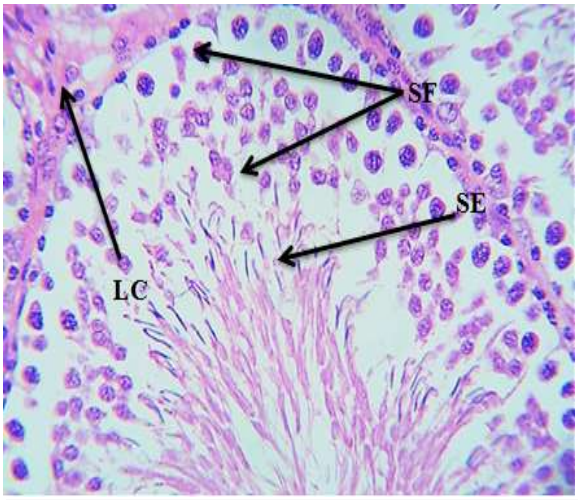


Image 3: Testicular section of the group treated with lead acetate and dried apricot fruit extract showing stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

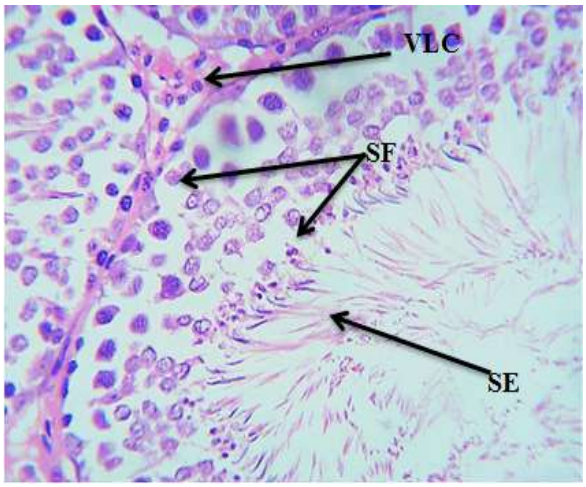


Image 4: Testicular section of the group treated with lead acetate and DHEA showing stages of spermatogenesis (SF) and mature spermatozoa (SE), with vacillation in Leydig cells (VLC). H&E, 400×.

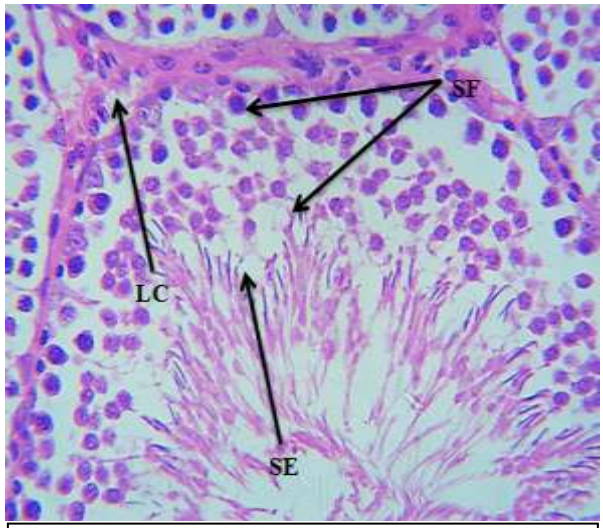


Image 5: Testicular section of the group treated with dried apricot fruit extract showing stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

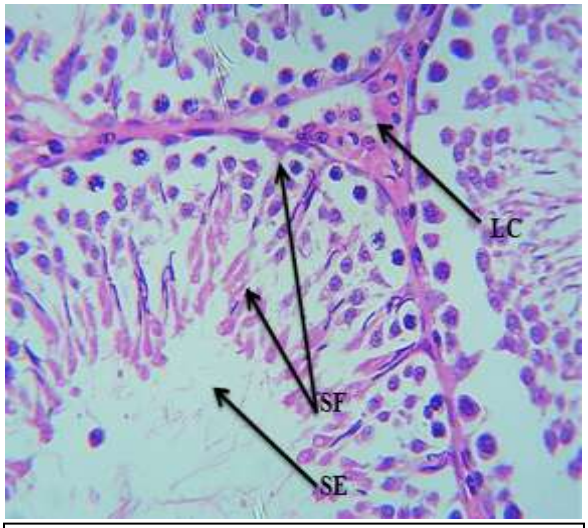


Image 6: : Testicular section of the group treated with DHEA showing weak stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

**3.2- Sperm landmarks**

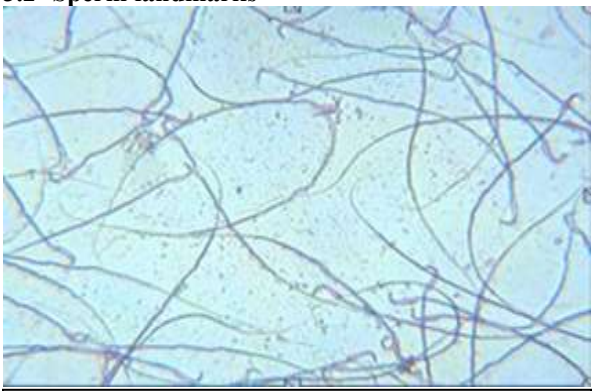

Image (7) shows the normal shape of the control group sperm.

Image (8) The lead acetate treatment group shows the twisted shape of the sperm tail in addition to the abnormal shape..

Image (9) shows the group treated with lead acetate and dosed with Dehydroepiandrosterone, illustrating the survival of a number of sperm with a coiled tail.

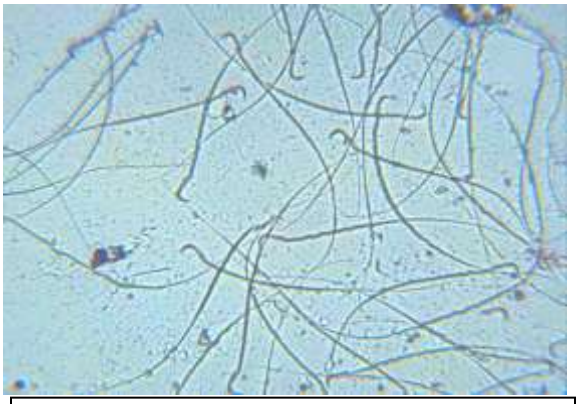

Image (10) The group treated with lead acetate and given a dose of dried apricot fruit extract shows the normal shape of the sperm.

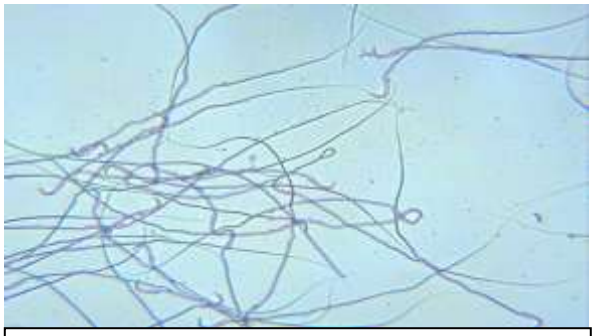

Image (11) The group given a dose of dehydroepiandrosterone only, the sperm appear normal.

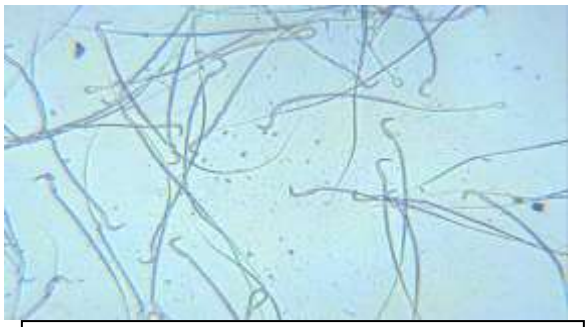

Image (12) The group that was given a dose of dried apricot fruit extract only, the sperm appear normal..

**3.3- Biochemical and Hormonal Parameters**

**Table (1)** shows that the treatment of rats with lead acetate led to a significant increase (P≤0.05) in the oxidative stress index, in addition to a decrease in antioxidant indicators compared to the control group, while the treatment of rats treated with lead acetate and doused with DHEA and dried apricot fruit extract led to the return of the indicators to their near-normal state.

| Standards / Groups | 8-OHdG ng/ml | SOD U/ml | GPx U/L |
|---|---|---|---|
| **Control group** | **61.60 ± 2.50 d** | **51.64 ± 2.04 a** | **1.518 ± 0.564 a** |
| **Lead acetate** | **104.54 ± 7.25 b** | **34.52 ± 4.54 d** | **0.427 ± 0.094 d** |
| **Lead acetate group treated with DHEA** | **91.80 ± 4.47 c** | **43.37 ± 4.66 b** | **0.654 ± 0.115 c** |
| **Lead acetate group treated with dried apricot fruit extract** | **89.39 ± 7.52 c** | **37.87 ± 6.92 c** | **0.713 ± 0.107 c** |
| **Lead acetate group treated with dried apricot fruit extract and DHEA** | **90.47 ± 7.77 c** | **42.05 ± 3.22 b** | **1.595 ± 0.329 a** |
| **DHEA-treated group** | **125.81 ± 8.70 a** | **41.97 ± 2.91 b** | **1.640 ± 0.083 a** |
| **Dried apricot fruit extract–treated group** | **91.09 ± 8.75 c** | **40.48 ± 3.32 b** | **1.395 ± 0.185 b** |

**Table (2)** shows that treating rats with lead acetate resulted in a significant decrease of (P≤ 0.05) in the level of sex hormones such as testosterone, ICSH, SSH, compared to the control group, while treating the rats with lead acetate and dosing them with DHEA and dried apricot fruit extract resulted in the indicators returning to almost normal.

| Standards / Groups | Testerone Hormone pg/ml | ICSH mlU/ml | SSH mlU/ml |
|---|---|---|---|
| **Control group** | **836.6 ± 57.8 a** | **4.460 ± 0.774 e** | **4.348 ± 0.683 c** |
| **Lead acetate** | **382.1 ± 84.3 e** | **2.637 ± 1.004 f** | **4.666 ± 0.714 bc** |
| **Lead acetate group treated with DHEA** | **697.7 ± 90.7b** | **9.501 ± 1.120 d** | **5.810 ± 0.975 a** |

| | | | |
|---|---|---|---|
| **Lead acetate group treated with dried apricot fruit extract** | **511.8 ± 44.9 cd** | **4.176 ± 0.332 e** | **5.078 ± 1.036 b** |
| **Lead acetate group treated with dried apricot fruit extract and DHEA** | **474.1 ± 70.3 d** | **14.149 ± 1.951 b** | **6.160 ± 1.086 a** |
| **DHEA-treated group** | **295.9 ± 33.0 f** | **11.293 ± 1.339 c** | **5.945 ± 0.599 a** |
| **Dried apricot fruit extract–treated group** | **551.2 ± 51.8 c** | **17.530 ± 2.401 a** | **5.584 ± 0.185 ab** |

## 4. Discussion

These results indicate clear tissue damage to the testicular tissue, in addition to a change in sperm characteristics. This indicates an imbalance in the oxidation-reduction balance as a result of lead exposure, which is consistent with what multiple studies have indicated, confirming that lead is a heavy metal capable of stimulating the production of reactive oxygen species (ROS) and weakening the antioxidant defense system in various body tissues [11] . This oxidative disorder is attributed to the ability of lead to enter the body through the digestive system, through respiration, or through the skin and then pass into the blood, where it binds to the sulfhydryl (SH-) groups of proteins and enzymes, leading to inhibition of the effectiveness of antioxidant enzymes and disruption of their vital functions, in addition to displacing the mineral elements necessary for the activity of some of these enzymes, such as zinc and copper in the SOD enzyme, which leads to the accumulation of free radicals inside cells [12] .

The testicle is an organ that is highly sensitive to environmental changes and toxicity, especially exposure to heavy metals such as lead, because the process of spermatogenesis requires a delicate balance between the structural integrity of the seminiferous tubules, the efficiency of germ cells, and the function of Leydig cells, which are responsible for producing male sex hormones. This leads to the stimulation of oxidative stress and an increase in the production of reactive oxygen species (ROS), which in turn leads to widespread cellular damage involving membrane lipids, proteins, intracellular DNA, and inflammation, which in turn leads to sperm death and a decrease in mature sperm [13] . Lead weakens the activity of these cells and inhibits the enzymes responsible for testosterone synthesis, leading to a decrease in its levels within the testicle. Testosterone is an essential element in supporting the germinal epithelium and regulating the function of Sertoli cells , therefore, any disruption in its secretion negatively affects the regulation of the stages of spermatogenesis and its final characteristics [14] .

In comparison to some studies demonstrating broad protective effects of synthetic antioxidants such as vitamin E and kafempferol against lead-induced oxidative damage, here we tested DHEA and dried apricot fruit extract with different antioxidant modes . These results are consistent with studies that indicated that DHEA has a protective role in reducing DNA damage and improving the cellular environment that supports male fertility [15] . The study results also showed that treatment with apricot fruit extract (1.5 ml/animal) contributed to reducing oxidation products and increasing antioxidant levels. This is attributed to the presence of phenolic compounds, carotenoids, and antioxidant vitamins in apricots, which work to scavenge free radicals and reduce lipid peroxidation, in addition to stimulating antioxidant enzymes [16] . Recent studies have confirmed that antioxidant-rich fruit extracts reduce markers of DNA damage such as OHdG-8 in animal models exposed to oxidative stress [17,18] .

In the current study, testosterone, ICSH, and SSH levels were significantly reduced in the lead acetate treatment group compared to the control group, consistent with scientific studies indicating that lead exposure leads to disturbances in Leydig function and seminiferous epithelial cells and reduces testosterone production by negatively affecting the efficiency of the hypothalamic-pituitary-testicular axis, which is reflected in decreased testosterone secretion [19] . Lead exposure leads to degenerative changes in testicular tissue, including atrophy of the seminiferous tubules and loss of spermatogenesis, which negatively impacts the efficiency of interstitial cells (Leydig cells) and consequently reduces testosterone secretion. The decreased levels of testosterone, ICSH, and SSH in lead poisoning are also associated with increased oxidative stress within testicular tissue, leading to increased DNA and cell membrane damage and reduced mitochondrial function. This mechanism is supported by recent studies examining the role of oxidative stress in causing hormonal imbalances and male infertility [20,21] .

Hormones such as DHEA are capable of improving the hormonal environment within the testes and reducing some manifestations of indirect oxidative stress, thus supporting sperm production and quality, as indicated by Isidori et al. [22] . The current results also showed that treatment with apricot fruit extract led to a moderately significant improvement in testosterone, ICSH, and SSH levels compared to the lead group. Scientific studies indicate that plant compounds rich in antioxidants, such as flavonoids and vitamins found in fruits, can contribute to reducing oxidative stress within reproductive tissues, thereby limiting cell damage and supporting hormonal functions, which is reflected positively in sex hormone levels and sperm characteristics [23].

## 5. Conclusion

The current study shows that exposure to lead acetate causes acute reproductive toxicity in male albino rats, manifested by oxidative DNA damage, disruption of the antioxidant defense mechanism, disturbance of reproductive hormone levels, and histological changes in the testes. Notably, extracts of Dehydroepiandrosterone and dried apricot fruit, individually and in combination, contributed to reducing many of the side effects. Their protective responses against the toxic damage of lead acetate were particularly noteworthy.

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