RESEARCH PAPER

Dehydroepiandrosterone and dried apricot fruit extract as protective agents against lead-induced reproductive toxicity in male albino rats

Rejan Ameen Mustafa[1], Qasim Azeez Razooqi[2]

[1,2]Department of Biology, College of Education for Pure Sciences, Tikrit University, Iraq.

Corresponding author Email: ramueps50@st.tu.edu.iq

Abstract

Lead is one of the most striking environmental health issues because of its well-established toxic effect on male reproductive system, especially through oxidative stress and hormone imbalance. The aim of this study was to investigate and compare the protective potential of dehydroepiandrosterone (DHEA) and dried apricot fruit extract against lead-induced reproductive toxicity in male albino rats. A total of 35 male rats were equally divided into seven groups (n = 5 in each group) as; control, lead acetate-treated and animals treated with DHEA and/or dried apricot fruit extract for a period of 35 days. Serum 8-hydroxy-2′-deoxyguanosine (8-OHdG), reproductive hormones (ICSH, SSH and testosterone), and antioxidant enzymes (superoxide dismutase and glutathione peroxidase) were detected by enzyme ELISA. Pathological analysis of the testicular tissue was also conducted. Lead acetate exposure induced significant elevation in oxidative DNA damage, disruption of antioxidant enzyme activities, disruption of reproductive hormone levels, and histological changes with impairment of spermatogenic tissue and seminiferous tubules degeneration. However, treatment with DHEA and dried apricot fruit extract alone and in a more efficient way along with each other resulted in marked improvement in these biochemical as well as histopathological parameters. In brief, DHEA and dried apricot fruit extract exert protective effects against lead-induced reproductive toxicity, which is probably attributed to antioxidant defense improvement and the maintenance of the structure and function of testis.

Keywords: *Lead acetate, Dehydroepiandrosterone, Dried apricot fruit extract, Oxidative stress, Male reproductive toxicity*

How to cite this article: Mustafa RA, Razooqi QA. Dehydroepiandrosterone and dried apricot fruit extract as protective agents against lead-induced reproductive toxicity in male albino rats. Int J Drug Deliv Technol. 2026;16(8s): 243-252; DOI: 10.25258/ijddt.16.8s.25

1. Introduction

The exposure to environmental heavy metals has become a serious public health problem globally, and lead as one of the most widely distributed toxic pollutants. Lead is a naturally occurring heavy metal commonly used in battery production, paint and gas. But there's serious health risks that arise when it accumulates in the environment and is taken up by the human or animal body [1]. Lead has many toxic activities, and lead-induced oxidative stress is considered as one of the major causes of cellular damage in various organs such as liver, kidney, brain and reproductive organs [2]. The reproductive system of males in particular is very susceptible to oxidation because sperm membranes are rich in polyunsaturated fatty acids and because spermatogenesis is a very complex process that needs cellular differentiation as well as hormonal regulation [3].

Oxidative stress takes place when the equilibrium between production of reactive oxygen species (ROS) and antioxidant defenses is disturbed leading to cellular and molecular damages. Lead has been reported to enhance ROS production, reduce endogenous antioxidants and enzymatic function resulting in lipid peroxidation, DNA damage, and protein oxidation [4]. In the testis, this leads to impaired spermatogenesis, seminiferous tubule degeneration, germ cell apoptosis and altered Leydig cell functioning. Therefore, low sperm count, poor motility and morphology along with significant shifts in the levels of testosterone (T), follicle stimulating hormone (ICSH) and luteinizing hormone (SSH) have been frequently reported following lead exposure. This lead exposure-mediated oxidative altered status could eventually affect male fertility and reproductive health, highlighting the imperative for interventions that can counteract lead-induced oxidative damage [5,6].

In recent years, much attention has been paid to natural and synthetic antioxidants as a potential protective agent against toxicity induced by heavy metals. Of those agents, Dehydroepiandrosterone (DHEA) has been considered because of its numerous biological roles. DHEA is a steroid hormone that is produced by the adrenal glands and is naturally present in the body [7]. It is a precursor of both female and male sex hormones. In addition to steroidogenic activity, DHEA has strong antioxidative and anti-inflammatory effects that have been shown to enhance the cellular defense against oxidative stress. Some research has indicated that DHEA could increase the activities of antioxidant enzymes as well as decrease lipid peroxidation and protect testis function under oxidative stress and may be a potential candidate for the protection of reproduction health [8,9].

Conversely, natural plant extracts have been demonstrated to possess promising effects in reducing oxidative stress and improving reproduction; they have drawn increasing attention for novel dietary interventions [10]. Apricot fruit extract (adj) known to contain high concentrations of vitamins, carotenoids, polyphenols and other bioactive molecules such as antioxidants. Such components can quench free radicals, regulate antioxidant enzymes and attenuate oxidative injury of DNA and plasma membrane [11]. The supplementation of experimental models with dried apricot extract has been correlated with an improvement in sperm parameters, Sertoli and Leydig protection function as well as an increased spermatogenesis. Because natural antioxidants and some compounds such as DHEA might exert synergistic effects, they can additionally provide protection of the male reproductive system from toxic exposure [12].

Although individual antioxidants have been increasingly reported in literature, few articles exist on combination of DHEA with plant extracts against lead induced reproductive toxicity. It is important to know the protective mechanisms of drugs and a combination of drugs in order to mitigate adverse effects of pollutants and occupational exposure to toxic metals [13]. Animal experimental models, including those based on male albino rats are available to study the effects of these forms in a controlled environment and provide intensive biochemical, hormonal and histopathological information [14]. Variables like oxidative stress markers (8-hydroxy-2'-deoxyguanosine), antioxidant enzyme activities (superoxide dismutase, glutathione peroxidase) and reproductive hormone levels offer a broad-spectrum idea of testicular function and cell damage during toxic circumstances [15]. This study does not only contribute to the knowledge in reproductive toxicology but may also offer promising therapeutic approaches for reducing heavy metal-induced male infertility. The aim of this study was to investigate the impact of Dehydroepiandrosterone (DHEA) and dried apricot fruit extract singly or in combination against oxidative stress and testicular injury induced by lead in male albino rats. The purpose will be to estimate their effectiveness in maintaining the hormonal balance, anti-oxidative status and normal testicular histology.

2. Materials and Methods

2.1 Experimental Animals

In the present investigation, 35 male albino rats were used and randomly put into seven different groups (n = 5 in every group) so that the body weights of the rats in all groups were identical. The animals were kept in a standard experimental setting and had access to food and water at all times during the study duration.

2.2 Experimental Design and Grouping

On October 6, 2025, the experimental animals were randomly divided into seven groups, with five rats in each group and administered the treatment for a total of 35 days.. Animals within each group were selected to have comparable body weights .The groups were arranged as follows:

- **Control group (A):** This group received distilled water and a standard diet daily for 35 days.
- **Lead acetate–induced oxidative stress group (B):** This group was administered lead acetate at a dose of 50 mg/kg body weight orally for 35 days.
- **Oxidative stress group treated with DHEA (C):** 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.
- **Oxidative stress group treated with dried apricot fruit extract (D):** 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.

- **Oxidative stress group treated with DHEA and dried apricot fruit extract (E):** 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.
- **DHEA-treated group (F):** This group was administered DHEA orally at a dose of 4 mg/kg body weight daily throughout the experimental period.
- **Dried apricot fruit extract–treated group (G):** This group received dried apricot fruit extract orally at a dose of 1.5 mL/animal daily throughout the experimental period.

2.3 Biochemical Analysis

After the experiment was over, blood samples were taken from each of the animals. We used commercial ELISA kits (Fine Test, China) to measure serum concentrations of the following factors, as shown in Table 1.

Table 1: Studied Parameters

Parameter	Abbreviation	Unit
8-hydroxy-2'-deoxyguanosine	8-OHdG	ng/mL
Interstitial Cell-Stimulating Hormone	ICSH	mIU/mL
Sperm Stimulating Hormone	SSH	mIU/mL
Testosterone	T	ng/dL
Superoxide dismutase	SOD	U/mL
Glutathione peroxidase	GPx	U/mL

2.4 Histopathological Examination

Testes were meticulously excised, preserved in 10% formalin, and prepared for paraffin embedding. We used Hematoxylin & Eosin (H&E) to stain 5 µm-thick parts and looked at them under a light microscope. The research concentrated on the seminiferous tubules, various phases of spermatogenesis, mature spermatozoa, and the morphology of Leydig cells.

2.5 Statistical Analysis

Data are expressed as mean ± SD (Mean ± SD). All data analysis was conducted with the SPSS software (version 23). The differences between groups were checked by one-way ANOVA analysis followed by the Tukey's multiple comparisons test. $P < 0.05$ was considered as statistically significant.

3. Results

3.1 Biochemical and Hormonal Parameters

3.1.1 Oxidative Stress Marker (8-OHdG)

Table 2 and Figure 1 serum levels of 8-hydroxy-2'-deoxyguanosine (8-OHdG) were significantly higher in lead acetate-treated group (B) compared to control group (A), indicating an increase in oxidative DNA damage. Furthermore, the levels of 8-OHdG were lower in lead-intoxicated rats treated with DHEA (C), dried apricot fruit extract (D) or both combined (E) compared to Pb-only group, but still remained higher from those found in Pb-alone treated animals being DHEA alone more significantly higher than all treatments. Moderate antioxidant protection was found in G, which receives only the dried apricot extract, as evidenced by a decrease of 8-OHdG to levels lower than other lead-exposed groups.

Table 2: Oxidative Stress Marker (8-OHdG) Levels

Parameter	Groups	Mean ± SD	P-value
8-OHdG	A	61.60 ± 2.50	0.01
	B	104.54 ± 7.25	
	C	91.80 ± 4.47	
	D	89.39 ± 7.52	
	E	90.47 ± 7.77	
	F	125.81 ± 8.70	
	G	91.09 ± 8.75	

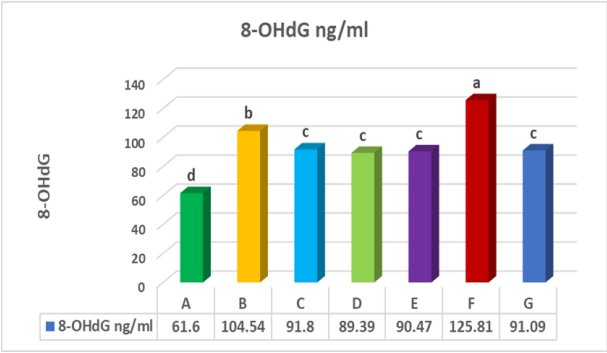

Figure 1: 8-hydroxy-2'-deoxyguanosine (8-OHdG) Level in the Studied Groups

3.1.2 Reproductive Hormones

The effect of lead exposure on Interstitial Cell-Stimulating Hormone (ICSH) and Sperm Stimulating Hormone (SSH) are represented in the Table 3. ICSH was reduced in the group of lead acetate-treated rats (B) compared to controls, while DHEA treatment alone or combined with dried apricot extract (C, E) increased ICSH levels significantly higher than control value.

Concurrently, SSH levels were moderately increased in lead-treated group (B) and were significantly modulated by DHEA as well as dried apricot agents.

Testosterone (T) levels Depicted in Figure (2), a considerable reduction was observed in group B as compared to group A. DHEA (C and F) supplementation significantly reversed the levels of testosterone, while dried apricot extract (D, G) moderate increase in testosterone secretion. Partial recovery was noted (E), and the levels were not recovered to the extent of the control group.

Table 2: Reproductive Hormones

Parameter	Groups	Mean ± SD	P-value
ICSH	A	4.46 ± 0.77	0.01
	B	2.64 ± 1.00	
	C	9.50 ± 1.12	
	D	4.18 ± 0.33	
	E	14.15 ± 1.95	
	F	11.29 ± 1.34	
	G	17.53 ± 2.40	
SSH	A	4.35 ± 0.68	0.01
	B	4.67 ± 0.71	
	C	5.81 ± 0.98	
	D	5.08 ± 1.04	
	E	6.16 ± 1.09	
	F	5.95 ± 0.60	
	G	5.58 ± 0.81	
Testosterone (T)	A	836.6 ± 57.8	0.01
	B	382.1 ± 84.3	
	C	697.7 ± 90.7	
	D	511.8 ± 44.9	
	E	474.1 ± 70.3	
	F	295.9 ± 33.0	
	G	551.2 ± 51.8	

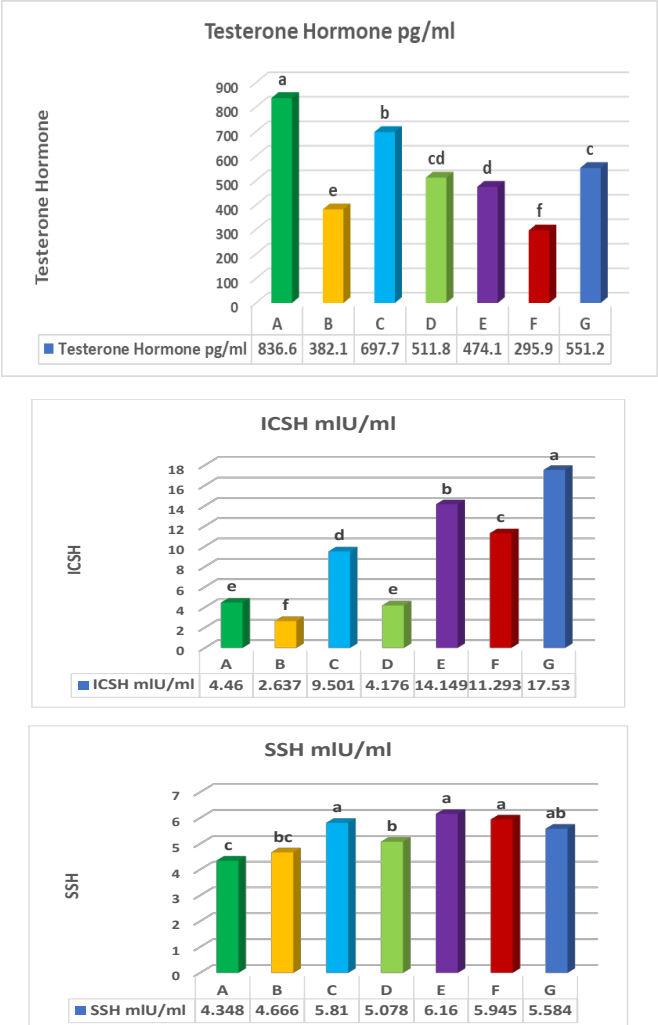

Figure 2: Reproductive Hormones Levels in the Studied Groups

3.1.3 Antioxidant Enzyme Activities

Table 3 and Figure 3 show that the activities of superoxide dismutase (SOD) and glutathione peroxidase (GPx) were much lower in the lead acetate group (B) than in the controls. This shows that the enzymatic antioxidant defenses were not working as well. Each participant's administration of DHEA (C, F) and dried apricot extract (D, G) significantly elevated both SOD and GPx activities in comparison to the lead-exposed group. The combination group (E) showed the most improvement in antioxidant enzyme activity, coming close to normal levels.

Table 3: Antioxidant Enzyme Activities

Parameter	Groups	Mean ± SD	P-value
SOD	A	51.64 ± 2.04	0.01
	B	34.52 ± 4.54	
	C	43.37 ± 4.66	
	D	37.87 ± 6.92	
	E	42.05 ± 3.22	
	F	41.97 ± 2.91	
	G	40.48 ± 3.32	
GPx	A	1.518 ± 0.564	0.01
	B	0.427 ± 0.095	
	C	0.654 ± 0.115	
	D	0.714 ± 0.108	
	E	1.595 ± 0.329	
	F	1.641 ± 0.083	
	G	1.395 ± 0.185	

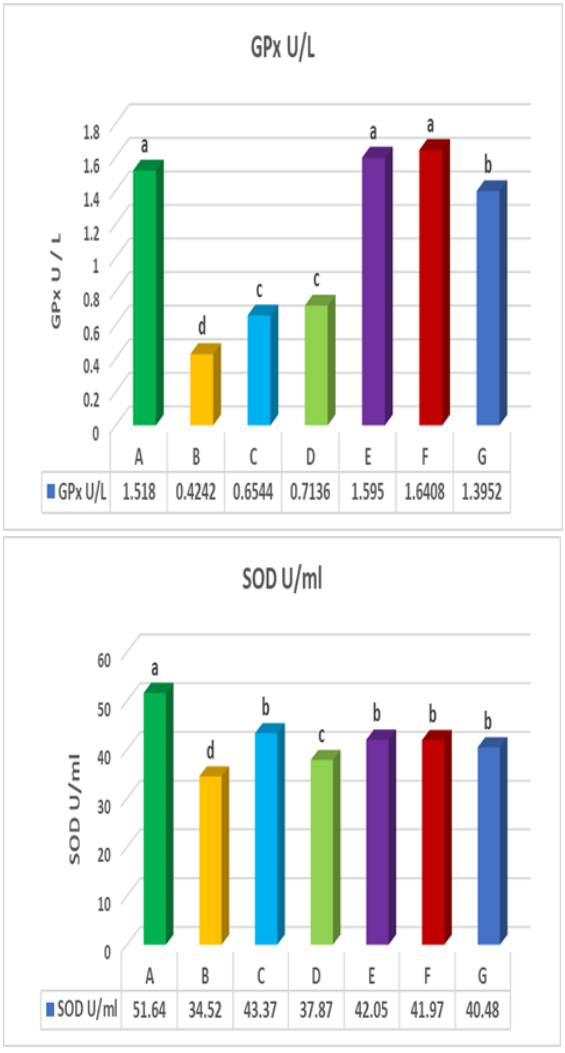

Figure 3: Antioxidant Enzyme Levels in Studied Groups

3.2 Histopathological Findings

3.2.1 Control Group

Testicular sections of the control group (Figure 4) displayed normal architecture with well-organized seminiferous tubules (ST) and clearly visible Leydig cells (LC). Spermatogenesis was normal, and mature spermatozoa (SE) were abundant.

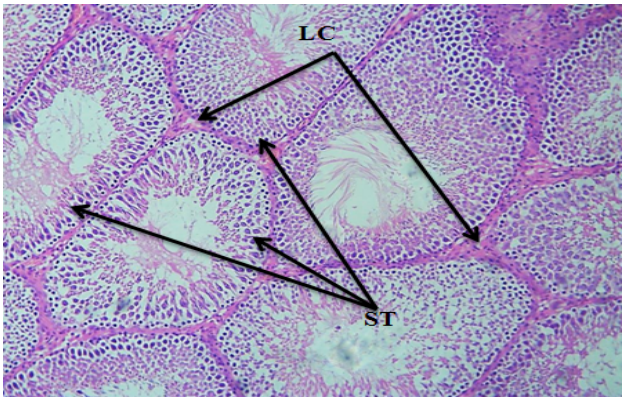

Figure 4: Testicular section of the control group showing seminiferous tubules (ST) with normal structure. Leydig cells (LC) are clearly visible. H&E, 100×.

3.2.2 Dried Apricot Fruit Extract Group

Rats treated with dried apricot fruit extract alone (Figure 5) exhibited intact seminiferous tubules with clear stages of spermatogenesis (SF) and abundant mature spermatozoa (SE). Leydig cells appeared normal, indicating no histopathological alterations due to the extract alone.

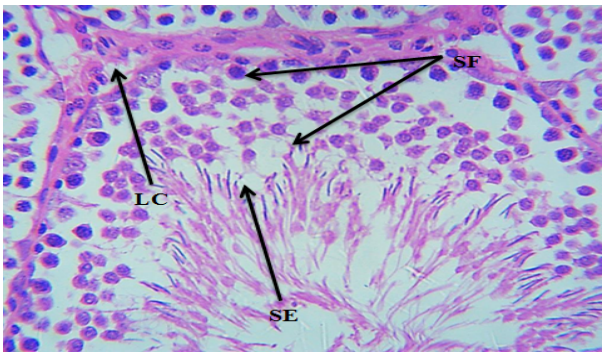

Figure 5: Testicular section of the group treated with dried apricot fruit extract showing stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

3.2.3 DHEA Group

The DHEA-only group (Figure 6) showed slightly weaker spermatogenesis stages (SF) and a reduced number of mature spermatozoa (SE), although Leydig cells (LC) maintained normal morphology.

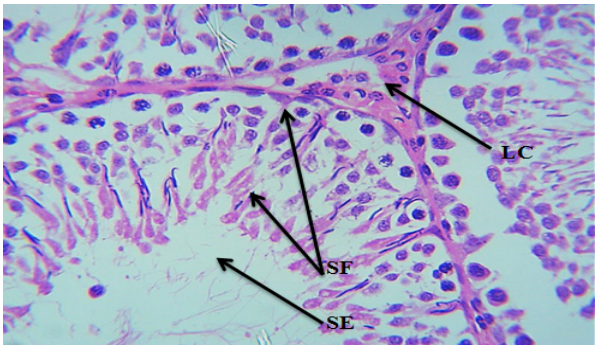

Figure 6: Testicular section of the group treated with DHEA showing weak stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

3.2.4 Lead Acetate Group

Lead acetate exposure (Figure 7) caused pronounced histopathological alterations, including accumulation of dense material (MU) within the seminiferous tubules and disruption of normal spermatogenesis (SF). Leydig cells appeared irregular, and spermatogenic activity was severely impaired.

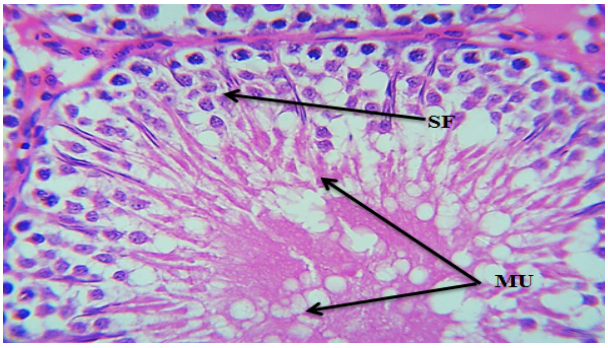

Figure 7: Testicular section of the lead acetate-treated group showing accumulation of dense material within seminiferous tubules (MU) and unclear spermatogenesis (SF). H&E, 400×.

3.2.5 Lead Acetate + Dried Apricot Fruit Extract Group

The combination of lead acetate with dried apricot fruit extract (Figure 8) resulted in noticeable improvement in seminiferous tubule architecture. Stages of spermatogenesis (SF) and mature spermatozoa (SE) were clearly visible, and Leydig cells (LC) appeared morphologically normal, suggesting a protective effect of the extract.

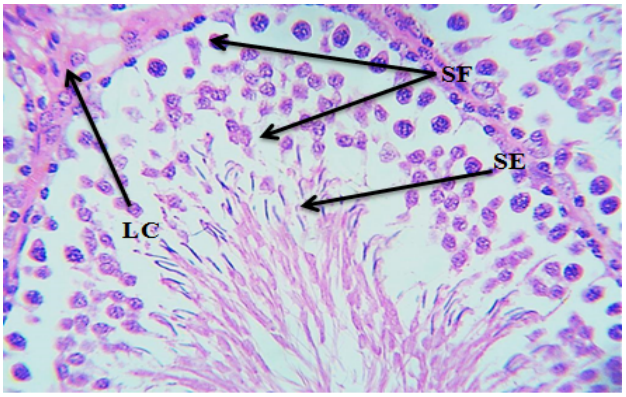

Figure 8: Testicular section of the group treated with lead acetate and dried apricot fruit extract showing stages of spermatogenesis (SF) and mature spermatozoa (SE). Leydig cells (LC) appear normal. H&E, 400×.

3.2.6 Lead Acetate + DHEA Group

In the group treated with lead acetate and DHEA (Figure 9), seminiferous tubules exhibited partial restoration of spermatogenesis (SF) and mature spermatozoa (SE). However, vacuolation in Leydig cells (VLC) was observed, indicating some residual cellular damage despite hormonal and antioxidant treatment.

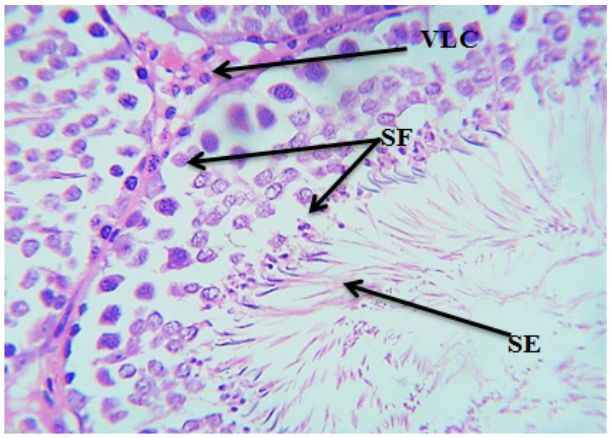

Figure 9: Testicular section of the group treated with lead acetate and DHEA showing stages of spermatogenesis (SF) and mature spermatozoa (SE), with vacuolation in Leydig cells (VLC). H&E, 400×.

4. Discussion

The current study showed that lead acetate causes remarkable testicular toxicity in male albino rats, represented by elevation of oxidative stress parameters, disturbance in hormones levels, inhibition of antioxidant enzymes and noticeable histopathological changes in the testis. These results are consistent with many lines of evidence showing that lead exposure is a strong inducer of oxidative stress and reproductive aberration in

experimental models. Oxidative stress is the consequence of increased ROS generation with the endogenous antioxidant defense system leading to cellular injury, lipid peroxidation, DNA damage and functional abnormalities in reproductive organs. Likewise, it is possible that increases in 8-OHdG observed here in lead-exposed rats reflect DNA damage from oxidative injury, and lend support to the contention that lead interferes with testicular genomic fidelity. This mode of action is consistent with those reported elsewhere in the literature for heavy metal-mediated oxidative stress on male fertility where ROS played a pivotal role in sperm quality deterioration and reproductive hormone-related disturbance [16].

Activities of major cellular antioxidant enzymes such as SOD and GPx was found to be significantly decreased by lead-induced oxidative stress in the current research. These are in line with previous studies that demonstrated that heavy metal poisonings lead to a diminution of antioxidant defense mechanisms, resulting in high ROS concentration and oxidative damage to the reproductive system. The protective property of different antioxidants on lead-induced reproductive toxicity has been extensively reported; for instance, the co-administration of plant extracts such as *Centella asiatica* offered protection against lead-induced oxidative stress and enhanced SOD activity and catalase hemesterase activities in addition to reversing changes observed in reproductive organ architecture [17]. In the same vein, hesperidin (natural antioxidant) was found to attenuate lead acetate-induced oxidative stress and decrease malondialdehyde levels, while enhancing testicular histopathology [18], thus reinforcing the predominant contribution of antioxidants in restraining lead toxicity.

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. Indeed, kaempferol alone or combined with vitamin E was able to reverse the inhibition of antioxidant enzymes and expression of steroidogenic genes in male rats exposed to lead acetate, thereby indicating potential use for flavonoid-based interventions in counteracting oxidative stress and disruption of steroidogenesis [19]. Although the present study does not allow us to draw direct parallels because different compounds were used, it serves as a corroborative example for the general postulation that antioxidant supplemented attenuate oxidative injury in male gonads.

Results of our studies indicated a significant decrease in serum testosterone level in the lead-treated group as compared to control, which is consistent with previous findings indicating that lead interferes with steroidogenesis and decreases circulating levels of testosterone. Imbalance of ICSH and SSH was also noted as a result of hypothalamic–pituitary–gonadal axis dysfunction. This hormonal imbalance is similar to that observed in other models of heavy metal poisoning, where serum testosterone and gonadotrophins were compromised with subsequent reduction in the weight of the testes and inhibition of spermiogenesis [20].

It was noted in our study that testosterone concentrations seem to be increased by DHEA treatment groups, likely because it is a precursor of androgens which are capable of influencing sex hormone biosynthesis. Although direct reproductive studies on DHEA in heavy-metal toxicity are sparse, DHEA has been shown to have antioxidant and modulatory effects on cellular oxidative status in various tissues, which also includes increased lipid peroxidation resistance and bettered antioxidant capacity in other experimental models [21]. These effects may be related to its efficacy in the partial reversal of altered hormone status in lead-exposed rats.

In addition, some studies on dietary antioxidants--e.g., carotenoid- and polyphenol-rich fruits also demonstrated hormonal protective effects. For example, *Prunus armeniaca* (apricot) has strong antioxidant activity and effectively ameliorates oxidative damage and prevents testicular histological deterioration in rats challenged with an oxidizing insult [22]. The antioxidant nature of our dried apricot fruit extract appears to have facilitated hormonal and its structural integrity by detoxifying ROS and assisting in endocrine activity.

Significant testicular histopathological alterations were produced by lead exposure, with intratubular accumulations and disturbed spermatogenesis, being consistent with data from other toxicological studies of lead and heavy metals. These abnormal changes were also accompanied by seminiferous epithelium degeneration, germ cell loss and

Leydig cell injury that would in turn have affected steroid production and antioxidant homeostasis [23].

Both untreated and treated groups exhibit modifications of seminiferous tubule architecture and stages of spermatogenesis, leading to the conclusion that structural repair was caused by biochemical improvements in antioxidant profile and hormone levels in association with DHEA as well as dried apricot extract treatment. This is consistent with the previous studies that showed that antioxidant supplementation of plant extracts or compounds ameliorated testicular tissue architecture of the toxin treated groups [24].

Although our findings are relatively consistent with the available literature indicating antioxidant protection from heavy metal-induced reproductive damage, some studies observed partial or inconsistent reversal of reproductive measures as a function of the type, dose and/or duration of exposure to antioxidants. For instance, *Moringa oleifera* leaf extract enhanced sperm quality and antioxidant status in lead-exposed rats although not all parameters were completely restored [25], which indicates that the effectiveness of antioxidants may vary according to the agent and experimental condition.

Also relevant are some reports on the biological activity of DHEA which show complex effects in reproductive tissues; for example, certain early research yielded evidence that administration of DHEA led to structural modifications in male reproductive organs under given experimental conditions, such as atrophy of seminiferous tubules [26]. Such disparities can be due to dose difference regimens, animal models utilized or the application/absence of other toxic insults suggestive of the necessary requirements for optimization of therapeutic protocols.

Conclusion

The current study shows that lead acetate exposure provokes severe reproductive toxicity in male albino rat which was evident through oxidative DNA damage, altered antioxidant defense mechanism, disrupted levels of reproductive hormones and drastic histopathological changes in testis. Elevation of 8-hydroxy-2′-deoxyguanosine and decrease of superoxide dismutase and glutathione peroxidase activities also indicate that oxidative stress is a key mechanism in lead-induced testicular injury. Furthermore, lead exposure led to a prominent disruption of the hypothalamic–pituitary–gonadal (HPG) axis, as evidenced by lowered circulating testosterone levels and altered gonadotropin secretion; such changes were histologically represented by compromised spermatogenesis and seminiferous tubular atrophy.

Significantly, extracts of dehydroepiandrosterone and dried apricot fruit, separately and in combination, reduced many of the side effects. Their defensive reactions were marked with amelioration of the antioxidant state, partial recovery of the hormonal profile and promising rehabilitation in testicular morphology. These findings indicate that dehydroepiandrosterone and dried apricot fruit extract could be potential protective agents against lead-induced reproductive toxicity, largely due to their antioxidative and tissue-protective effects.

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